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PYELORENAL BACKFLOW CLINICAL SIGNIFICANCE AND INTERPRETATION

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It has long been recognized that under certain conditions substances in the renal pelvis may enter the renal parenchyma and circulation Hinman[1] demonstrated that this could happen with pressure little if any greater than normal intrapelvic pressure A route by which this may happen is pyelorenal backflow—a general term applied to finding of urographic medium that has passed beyond the confines of the renal pelvis and calyces

The purpose of this paper is to emphasize the clinical importance of pyelorenal backflow from the standpoint of radiographic interpretation and its possible role in the pathogenesis of disease The channels by which backflow may occur and the roentgenological findings are briefly discussed, and illustrative cases are cited

DISCUSSION

In 1924 Hinman and Lee-Brown[2] recognized four types of renal backflow—pyelotubular, pyelointerstitial, pyelolymphatic and pyelovenous More recently Narath[3] has added a new nomenclature—pyelocanalicular backflow, pyelosinous transflow, sinolymphatic absorption and sinovenous ingression Of these, pyelosinous transflow and sinovenous ingression carry a different meaning and implication from that suggested by Hinman's classification

These various types of pyelorenal backflow are recognized by certain radiographic characteristics

Pyelotubular or pyelocanalicular backflow is recognized by a tuft of fine lines radiating from the end of the calyx, giving a brush-like characteristic often outlining the whole renculus belonging to this calyx (fig 1) No known pathologic significance can be attached to this finding An explanation of why the tubules fill with contrast medium is not easy, particularly when found on intravenous urograms Whether this results from stasis in the tubules, reabsorption, or a true backflow through the existing ducts of Bellini is not known

Pyelointerstitial backflow implies that medium has penetrated the stroma of the kidney and usually represents an extravasation or injury The contrast medium is interspersed in an irregular manner throughout the renal parenchyma (fig 2, *B*, broken arrow)

Pyelolymphatic backflow is observed when the lymphatics become filled with urographic medium and is recognized by fine streaks or thread-like channels passing from the fornix of a calyx toward the midline to the periaortic nodes

Accepted for publication November 16, 1956

[1] Hinman, F Principles and Practice of Urology Philadelphia W B Saunders Co, 1935

[2] Hinman, F and Lee Brown, R L J A M A, 82 607, 1924

[3] Narath, P A J Urol, 43 145, 1940

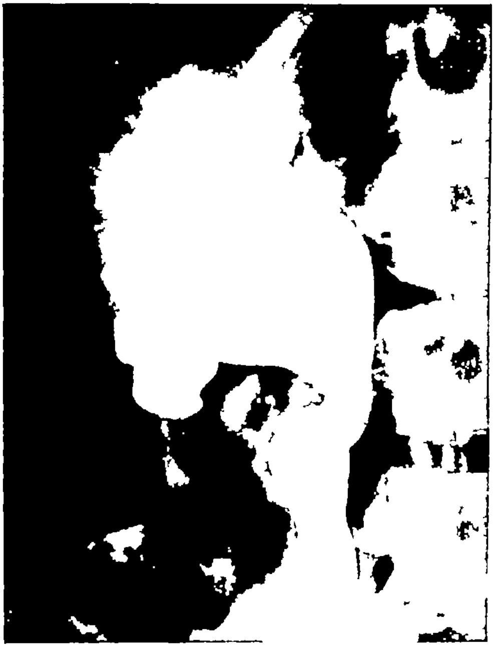

FIG 1 Pyelotubular backflow demonstrated by retrograde pyelogram in hydronephrotic kidney

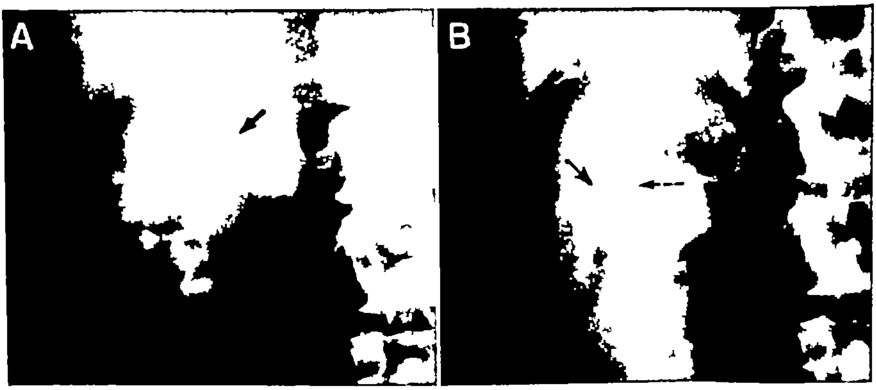

FIG 2 Excretory urograms demonstrate pyelorenal backflow in various forms *A* (broken arrow) pyelolymphatic backflow, (solid arrow), filling of interlobares vein *B* (broken arrow), pyelointerstitial backflow, (solid arrow), pyelovenous transflow

(fig 2, A, broken arrow and fig 5) This is believed to represent lymphatic permeation of medium from the sinus renalis

Pyelovenous backflow as observed by Hinman and Lee-Brown,[3] Lee-Brown and Laidley [4] and Fuchs[5] was thought to represent a tear or rupture of the fornical angle of a minor calyx into a peripapillary vein, thus the pyelographic picture produced would vary with the amount and extent of filling of the arcuatae, interlobares and interlobulares veins

[4] Lee Brown R K and Laidley J W S J A M A, 89 2091 1927
[5] Fuchs F Ztschr f urol Chir 27 257, 1929

The anatomical defect observed by Hinman and Lee-Brown to cause pyelovenous backflow implies a double injury simultaneously involving a calyx and vein (fig 2, *A*, solid arrow) Therefore, one should expect to demonstrate the site of injury in repeat pyelograms This is not usually the case, in fact, it is most difficult to demonstrate pyelovenous backflow from the same calyx on subsequent examinations even under greatly increased intrapelvic pressure When it does occur, it undoubtedly represents a true rupture of a fornical angle into a vein This double injury Narath prefers to call sinovenous ingression The conditions more commonly seen and loosely referred to as pyelovenous backflow he believes to be due to absorption through the mucosa of the fornix of a minor calyx under excessive pressure This, he has termed pyelovenous transflow (fig 2, *B*, solid arrow)

Early interest in pyelorenal backflow centered around its occurrence in retrograde pyelography Viethen[6] in 1931 recorded an instance of pyelotubular backflow during intravenous urograms Hendriock,[7] Narath,[8] and Olsson[9] have also reported various phases of pyelorenal backflow occurring with intravenous pyelograms Boyarsky[10] made a deliberate effort to produce extravasation following intravenous injection of contrast medium by prolonged abdominal compression He found an incidence of 2 5 per cent This parallels reports by Olsson of 2 5 per cent and Lindblom[11] of 1 6 per cent

CASE REPORTS

Case 1 AF 862408 A 40-year-old married man was admitted to the hospital with sudden onset of severe right flank pain which radiated toward the genitalia There was some urgency of urination There had been no previous episodes of similar pain His urologic history had been entirely normal to this point Past history revealed that he had served with the U S Army in the South Pacific In 1943 he was admitted to an army hospital and treated for amoebic dysentery In 1950 an appendectomy was done following an attack of right lower abdominal pain Four months later it was necessary to incise and drain a subhepatic amoebic abscess Lysis of adhesions for intestinal obstruction was done a year later Review of systems was negative

On physical examination his temperature was 98, pulse 70, respirations 20 He was found to be a well-developed, well-nourished man in acute distress There was severe pain in his right flank, with splinting and guarding of the right side of the abdomen The genitalia were normal

His urine was grossly clear with a specific gravity of 1 021 Albumin and sugar were negative Microscopic examination showed 40–50 red blood cells per high power field with an occasional white blood cell The white blood count was 21,800, hemoglobin 13 9 gm , nonprotein nitrogen 26 mg per cent, fasting blood sugar 111 mg per cent and uric acid 3 1 mg per cent A plain film of the abdomen

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[6] Viethen, H Rontgenpraxis, 3 370, 1931
[7] Hendriock, A Zentrbl f Chir , 61 1822, 1934
[8] Narath, P A J Urol , 39 65, 1938
[9] Olsson, O Acta radiol , suppl 70, 1948
[10] Boyarsky, S Personal communication
[11] Lindblom, A Acta radiol , 24 411, 1943

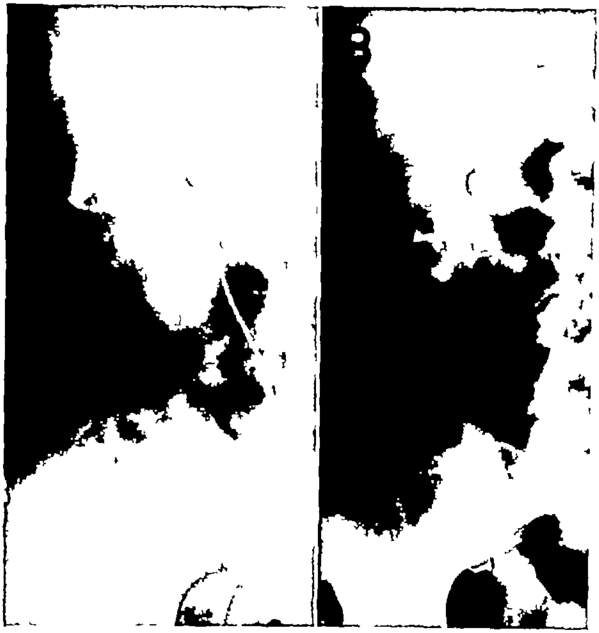


FIG 3 A, normal retrograde pyelogram made shortly after passage of ureteral calculus *B*, excretory urogram, made following day, shows normal configuration

showed the right psoas shadow to be indistinct A very small density was noticed in the region of the right ureterovesical junction Intravenous urograms showed prompt excretion of dye on the left side and a slight delay on the right with developing dilatation on successive films There was an irregular filling of the renal pelvis with what appeared to be extravasation of contrast medium from the calyceal system into the peripelvic space From the upper infundibulum there was extravasation toward the midline (fig 2, *A* and *B*) This appeared to be subcapsular

The day following admission his temperature rose to 101F and he passed a small calculus His temperature promptly subsided On cystoscopy the right ureteral orifice was slightly hyperemic No obstruction was met in passing a ureteral catheter and right retrograde pyelography was normal (fig 3, *A*) Intravenous urograms on the following day were normal (fig 3, *B*) His urine cleared The stone analysis showed a very slight trace of phosphorus and 4 plus oxalate He remained asymptomatic following passage of the calculus and was discharged on his fifth hospital day

Case 2 CR 860148 This was the third hospital admission for a 28 year-old man admitted because of chills, fever, gross hematuria, severe right costovertebral angle pain, generalized malaise, dysuria and nausea of 24 hours' duration The patient was first seen 8 months previously because of bilateral renal stones A left nephrolithotomy was done on that admission Four months later he returned with a small fragment of stone obstructing the left ureter which was removed by a left ureterolithotomy He had been on an anti-stone forming regimen consisting of high fluid intake and sodium phytate He had been studied extensively on his

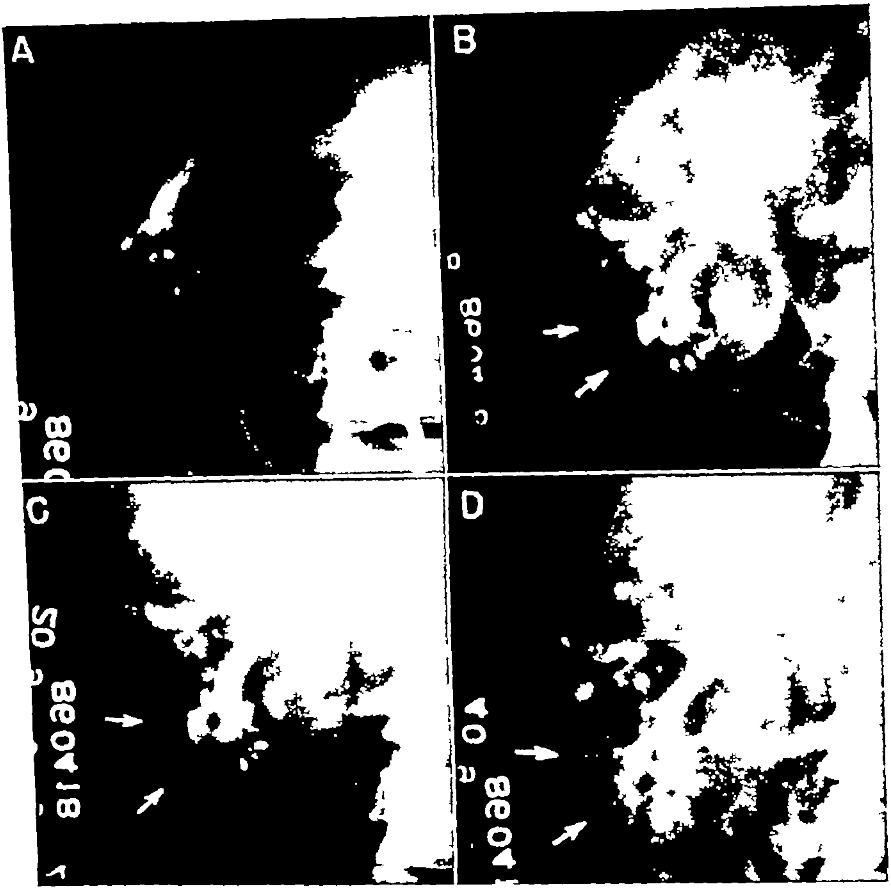
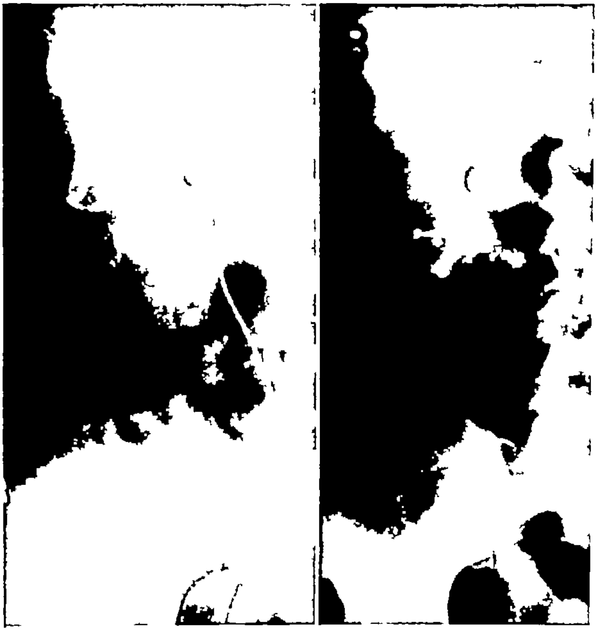


FIG 4 A, plain film shows numerous calcifications, most of which are in renal parenchyma, and branching calculus extending into lower calyces B, C D, excretory urogram shows progressive accumulation of contrast medium in tubules This was interpreted as calycectasis

previous admissions by Dr Albright's laboratory Repeated calcium and phosphorus studies were normal

On the present admission his temperature was 104F, blood pressure 100/50, pulse 100 and respirations 25 He was acutely ill His general physical examination revealed a congenital deformity of the jaw, thorax and abdomen There was marked tenderness to percussion and palpation over the right kidney The remainder of the physical examination was normal Laboratory studies showed a hemoglobin of 12 2 gm, white blood cells 16,500, nonprotein nitrogen 38 mg per cent, chlorides 96 mg per cent, sodium 128 mg per cent, potassium 3 4 mg per cent, total protein 6 6 gm, a/g ratio of 1 5, alkaline phosphatase 2 5 units, calcium 8 4 mg per cent, phosphorus 3 5 mg per cent, and uric acid 3 3 mg per cent His urine had a specific gravity of 1 022, 2 plus albumin and was negative for sugar There were 10 red blood cells and numerous white blood cells per high power field Urine cultures grew E coli and B pyocyaneus X-rays of the



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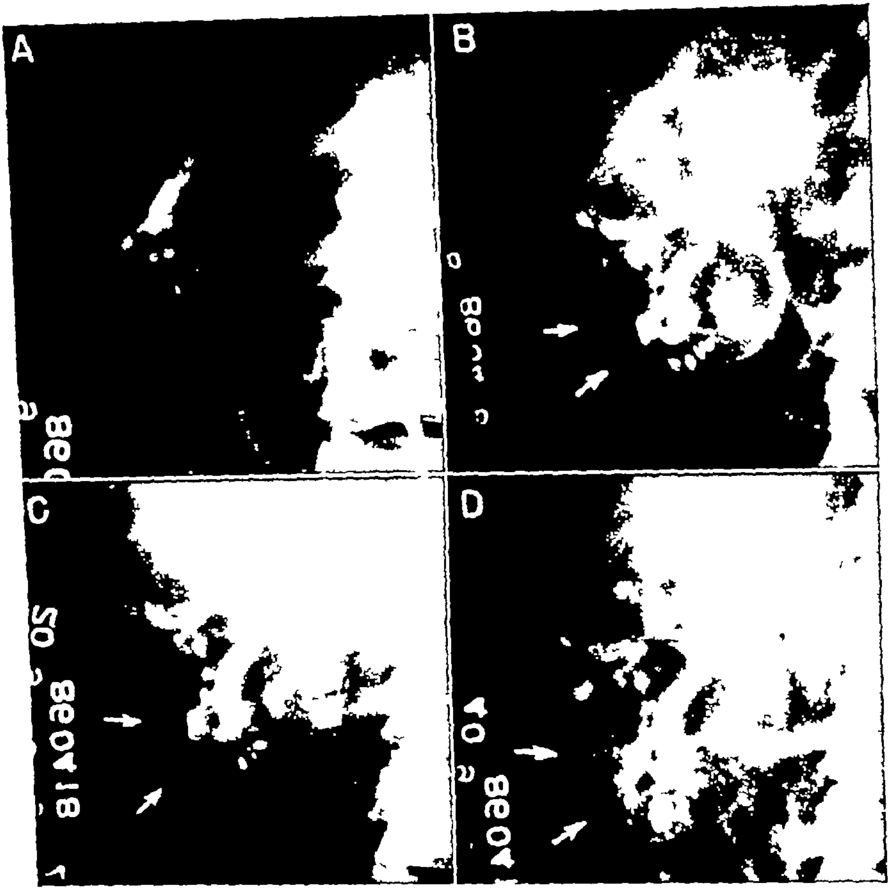

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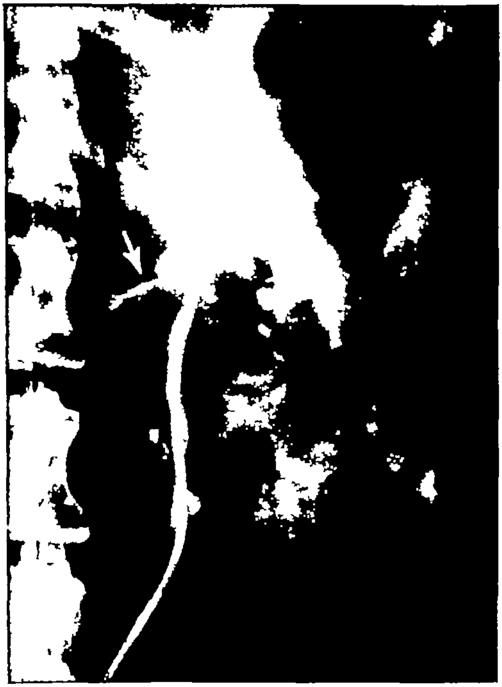

FIG 5 Pyelolymphatic backflow following retrograde pyelogram

abdomen showed numerous calcifications within the right renal shadow A large calculus was apparently in the pelvis and extended into the lower infundibulum The many smaller calcifications were presumed to be in the renal parenchyma (fig 4, *A*) Intravenous urograms showed slight left hydronephrosis There was delayed excretion of contrast medium on the right side with what appeared to be hydronephrotic calyces in the lower pole The radiologic interpretation of these films was obstruction to the lower infundibulum by the branching calculus causing calyceetasis of the lower calyces (fig 4, *B*, *C* and *D*)

While in the hospital he was given intravenous chloromycetin and intravenous fluids He remained febrile for 4 days His general condition gradually improved His urine cleared From the intravenous urograms it was felt that the large stone in the lower infundibulum was obstructing the lower pole, producing an infected calyceetasis which was responsible for the patient's symptoms On this basis the patient underwent surgery for removal of the large obstructing stone and as many of the smaller ones that might be free in the pelvis or calyceal system At surgery a small intrarenal pelvis was found and a nephrotomy was done over the lower pole of the kidney for removal of the stone On careful examination it was found that the lower calyces were not dilated and were perfectly normal Most of the calcifications noted in the x-rays were in the renal parenchyma and were not removed His postoperative course was uncomplicated and he was discharged on the eleventh postoperative day Stone analysis was phosphorus 4 plus calcium 4 plus ammonium 4 plus and magnesium 4 plus The patient was discharged on a high fluid low calcium diet and sodium phytate

CLINICAL SIGNIFICANCE

The exact role of pyelorenal backflow in absorption, infection, hydronephrosis, and chyluria is not clearly understood There is, however, sufficient evidence to suggest that it is an important factor in the pathogenesis of certain conditions

The frequency with which extravasations of varying degrees is seen following retrograde pyelograms must be kept in mind in choosing contrast media for that purpose Obviously any substance unsuitable for intravenous use should not be used or used only with great care The use of air which often is an extremely helpful diagnostic aid as well as sclerosing agents must be used cautiously

Infections may spread into the renal parenchyma, perirenal area or enter the bloodstream to produce bacteremia Parenchymal abscesses may occur following pyelointerstitial backflow or extravasation Subcapsular infections, perinephritis and perinephric abscess probably occur with pyelovenous or pyelolymphatic backflow The chills, fever and occasional bacteremia that follow retrograde pyelography undoubtedly result from extravasation of infected urine into the renal parenchyma, lymphatic or vascular system The spread of infection beyond the collecting system in septic obstructive uropathies probably occurs through these channels

The development of hydronephrotic atrophy is dependent on continued renal secretions in the presence of obstruction The mechanical and physiological processes involved in production of hydronephrotic atrophy are not entirely understood A contributing factor is pyelorenal backflow Increased secretory pressure promotes backflow, thus lowering the intrapelvic pressure This, in turn, permits more urine formation and secretion This process is repetitious and allows the development of huge hydronephrotic sacs Hinman considered back pressure the primary and essential factor in the production of hydronephrotic atrophy and backflow the secondary and controlling factor [1]

Wesson[12] stated that injection of the perirenal lymphatics indicated an open communication between the urinary tract and lymphatic system and that when such was present chyluria should exist Pyelo- or sinolymphatic backflow occurs not too infrequently and occurs in the absence of demonstrable chyluria Most instances of pyelolymphatic backflow represent an absorption by the lymphatics of urographic medium from the sinus renalis This undoubtedly is an important route of escape for fluids and solutes from the renal collecting system and probably is an important factor in the production of hydronephrotic atrophy However, one must consider the possibility of a direct communication between the lymphatics and urinary collecting system particularly when the findings can be reproduced on repeated examination

CLINICAL INTERPRETATION

Recognition of pyelorenal extravasation is essential for correct interpretation of pyelograms Pyelonephritis, tuberculosis, calycectasis, papillitis, and calyceal diverticulum must be differentiated

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[12] Wesson, M B Urol & Cutan Rev , 37 692, 1933

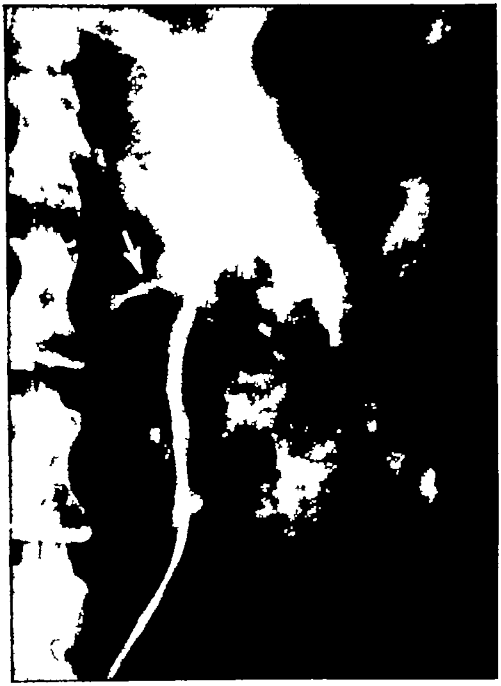

FIG 5 Pyelolymphatic backflow following retrograde pyelogram

abdomen showed numerous calcifications within the right renal shadow A large calculus was apparently in the pelvis and extended into the lower infundibulum The many smaller calcifications were presumed to be in the renal parenchyma (fig 4 *A*) Intravenous urograms showed slight left hydronephrosis There was delayed excretion of contrast medium on the right side with what appeared to be hydronephrotic calyces in the lower pole The radiologic interpretation of these films was obstruction to the lower infundibulum by the branching calculus causing calycectasis of the lower calyces (fig 4, *B*, *C* and *D*)

While in the hospital he was given intravenous chloromycetin and intravenous fluids He remained febrile for 4 days His general condition gradually improved His urine cleared From the intravenous urograms it was felt that the large stone in the lower infundibulum was obstructing the lower pole, producing an infected calycectasis which was responsible for the patient's symptoms On this basis the patient underwent surgery for removal of the large obstructing stone and as many of the smaller ones that might be free in the pelvis or calyceal system At surgery a small intrarenal pelvis was found and a nephrotomy was done over the lower pole of the kidney for removal of the stone On careful examination it was found that the lower calyces were not dilated and were perfectly normal Most of the calcifications noted in the x-rays were in the renal parenchyma and were not removed His postoperative course was uncomplicated and he was discharged on the eleventh postoperative day Stone analysis was phosphorus 4 plus, calcium 4 plus, ammonium 4 plus and magnesium 4 plus The patient was discharged on a high fluid, low calcium diet and sodium phytate

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A FUSED PELVIC (CAKE) KIDNEY

WILLIAM R SHILLER* AND OZRO B WISWELL

From the University of Texas Dental Branch, Houston, Texas

The literature reveals that the fused pelvic (cake) kidney is a very rare anomaly Huntington[1] alludes to a fused (cake) kidney in his Harvey Society lecture in 1907 The first apparent complete report was that of Looney and Dodd (1926) [2] Kron and Meranze (1949)[3] mentioned six previously reported cases, and added one of their own to bring the total to seven Since 1949, several authors have described pelvic kidneys, however, only Hanbury[4] and Saylor and Gordon[5] describe similar fused pelvic (cake) kidneys The two kidneys represented by Baurys[6] as being "cake" kidneys could hardly be considered such in view of the meager and nonconforming information given It can, therefore, be assumed that this is the tenth such case reported

The cake kidney is established as a fairly definite entity, being included in the classification of Lowsley and Kirwin [7]

DESCRIPTION

The histology of the cake kidney has been studied by McCrae[8] and by Saylor and Gordon [5] McCrae described immature glomeruli in his kidney Saylor and Gordon discovered infarction and thrombosis in their kidney which they felt was related to its abnormal blood supply

The embryological aspects were well elucidated by Huntington[1] and by Thompson and Pace [9] It is stated that in the development of the kidney the ureteric buds develop from the wolffian ducts at the 5 mm stage and branch into calyces at the 10 mm stage The kidney migrates upward and rotation medially occurs at the 14 mm stage, the adult position being reached at about the 25–30 mm stage It follows that, for some reason, further positional changes of these cake kidneys abruptly stop after the 10 mm stage in development

In the adult the cake kidney is consistently immature in position, form, blood supply, and ureter derivation All of the true cake kidneys described in the

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[3] Kron S D and Meranze D R Completely fused pelvic kidney J Urol , 62 278, 1949

[4] Hanbury W J Uncommon types of congenital renal abnormality Two cases Brit J Urol 21 237, 1949

[5] Saylor M and Gordon H Crossed renal ectopia with fusion complicated by massive infarction due to occlusive thrombosis of the aorta, case report J Urol , 65 968, 1951

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[8] McCrae L E Congenital solitary pelvic kidney J Urol , 48 58, 1942

[9] Thompson, G J and Pace J M Ectopic kidney Surg , Gynec & Obst , 64, 935, 1937

The first case illustrates the difficulty involved in interpretation particularly when such changes are seen on excretory urograms It demonstrates nicely the routes by which infection may spread into the renal parenchyma or perirenal space One can readily see the possible complications that might develop with extravasation of infected urine

The second case demonstrates pyelotubular backflow resembling calycectasis of the inferior calyceal group that led to an erroneous interpretation Retrograde pyelograms would have been most helpful in making a differentiation

Pyelovenous transflow with its thorn-like projection at the tip of a minor calyx may simulate early renal tuberculosis It is necessary to repeat pyelographic studies when the x-rays suggest some disease process not supported clinically It is unusual, indeed rare, to reproduce the same roentgenographic findings when such change or changes are due to pyelorenal backflow This is a most important consideration for when changes are due to some disease process they are usually reproduceable on repeated examinations, but when due to backflow it is most unusual to demonstrate the same findings

SUMMARY

Pyelotubular, pyelointerstitial, pyelolymphatic and pyelovenous backflow of Hinman or pyelosinus transflow and sinovenous ingression of Narath must be kept in mind for proper interpretation and evaluation of the roentgenographic findings seen on intravenous or retrograde pyelograms The x-ray changes produced by pyelorenal backflow can rarely be reproduced on subsequent examination

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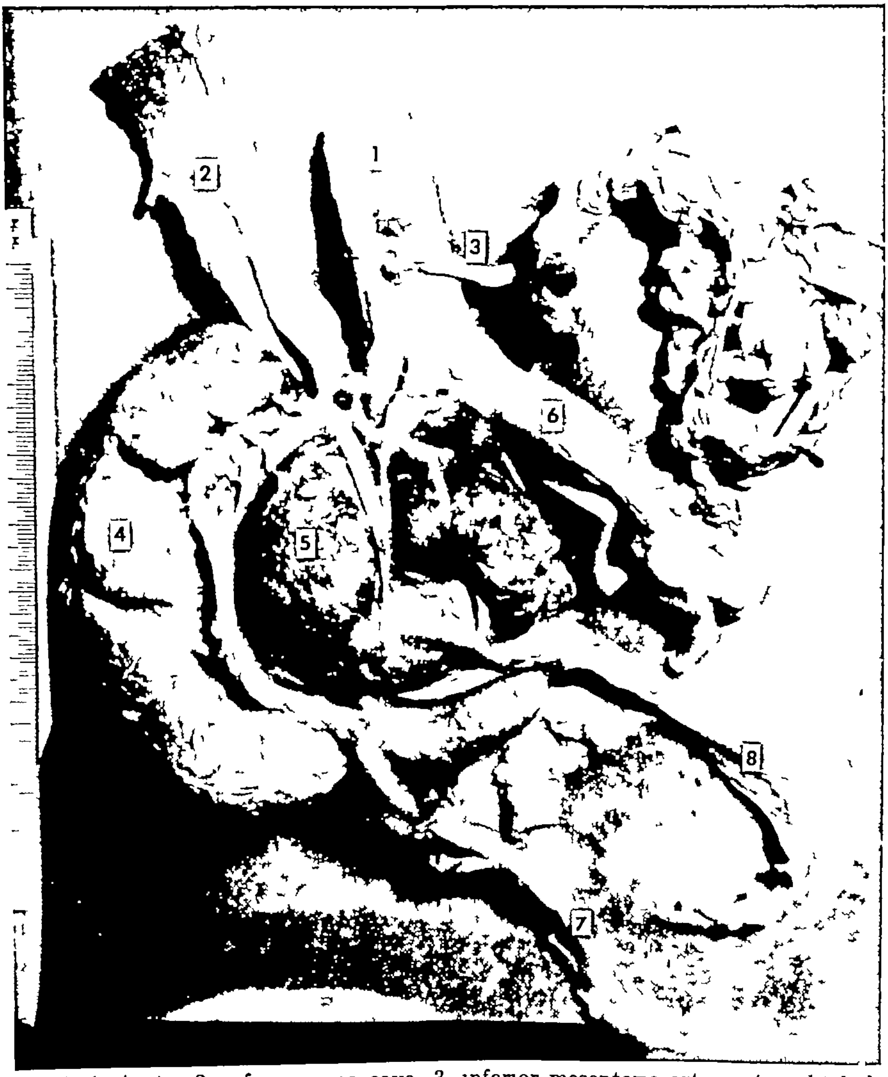

FIG 1 1, Aorta, 2, inferior vena cava, 3, inferior mesenteric artery, 4, right kidney mass, 5, left kidney mass, 6, common iliac vessels, 7, right ureter, 8, left ureter

literature except the one mentioned by Shoemaker and Braasch[10] were pelvic ectopias with blood supply derived from the aorta and vena cava near and at the bifurcation, and from the common iliac vessels This vascular arrangement mirrors the occurrence in embryonic development in that there vessels are the abnormally retained temporary vessels supplying the kidney during the stages of its ascent

The gross form of these cake kidneys is remarkably constant They are round, somewhat flattened masses with a lobulated anterior surface from which the ureters emerge and with a smooth concave posterior surface The ureters *per se*

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[10] Shoemaker, Rosemary and Braasch, W F Fused kidneys J Urol , 41 1, 1939

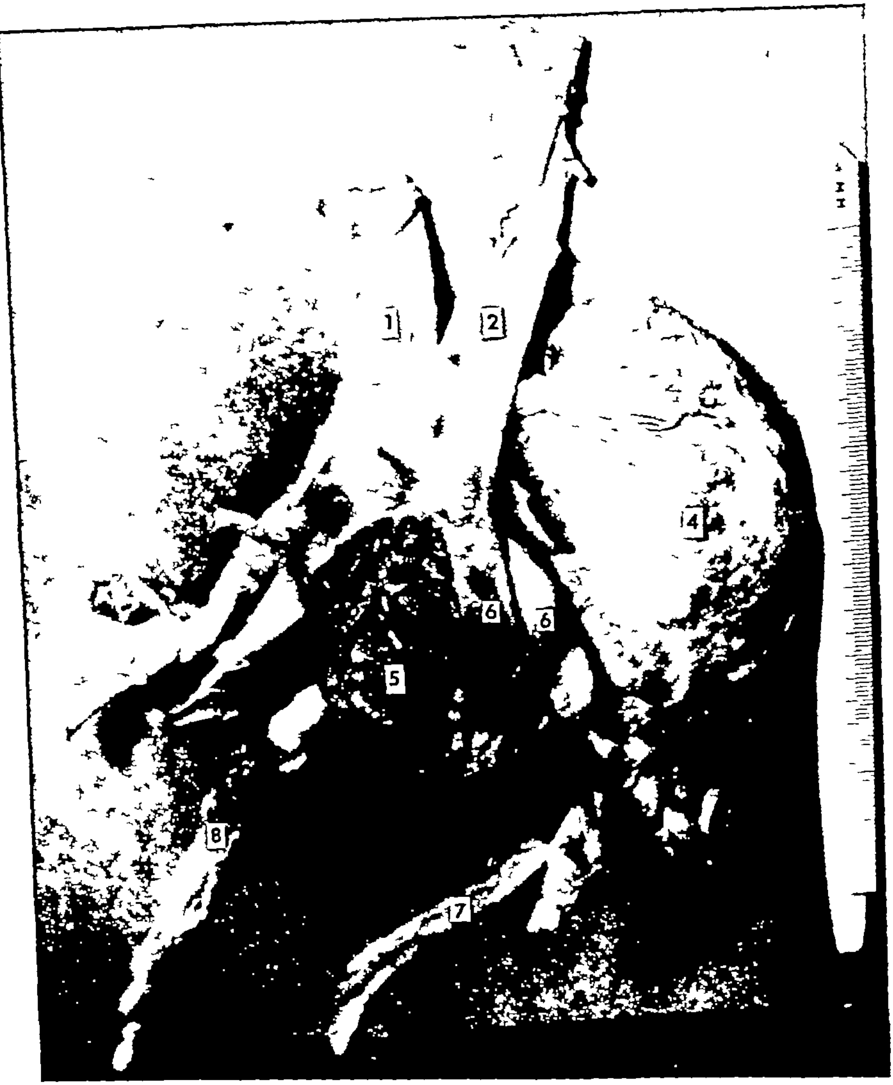

FIG 2 1, Aorta 2, inferior vena cava, 4, right kidney mass, 5, left kidney mass, 6, common iliac vessels, 7, right ureter, 8, left ureter

are usually normal, but their origin from extrarenal calyces on the anterior surface of the kidney is definitely atypical In all cases but one, there were two ureters with no definite renal pelvis McCrae[5] reported a case with but one ureter and a rather well defined renal pelvis

OBSERVATIONS

In a routine dissection of a 41-year-old Negro male, a grossly abnormal kidney was found This kidney mass was located on the right side with the superior limit just opposite the disc between the second and third lumbar vertebrae The inferior limit was found to extend into the true pelvis about 18 mm Posteriorly

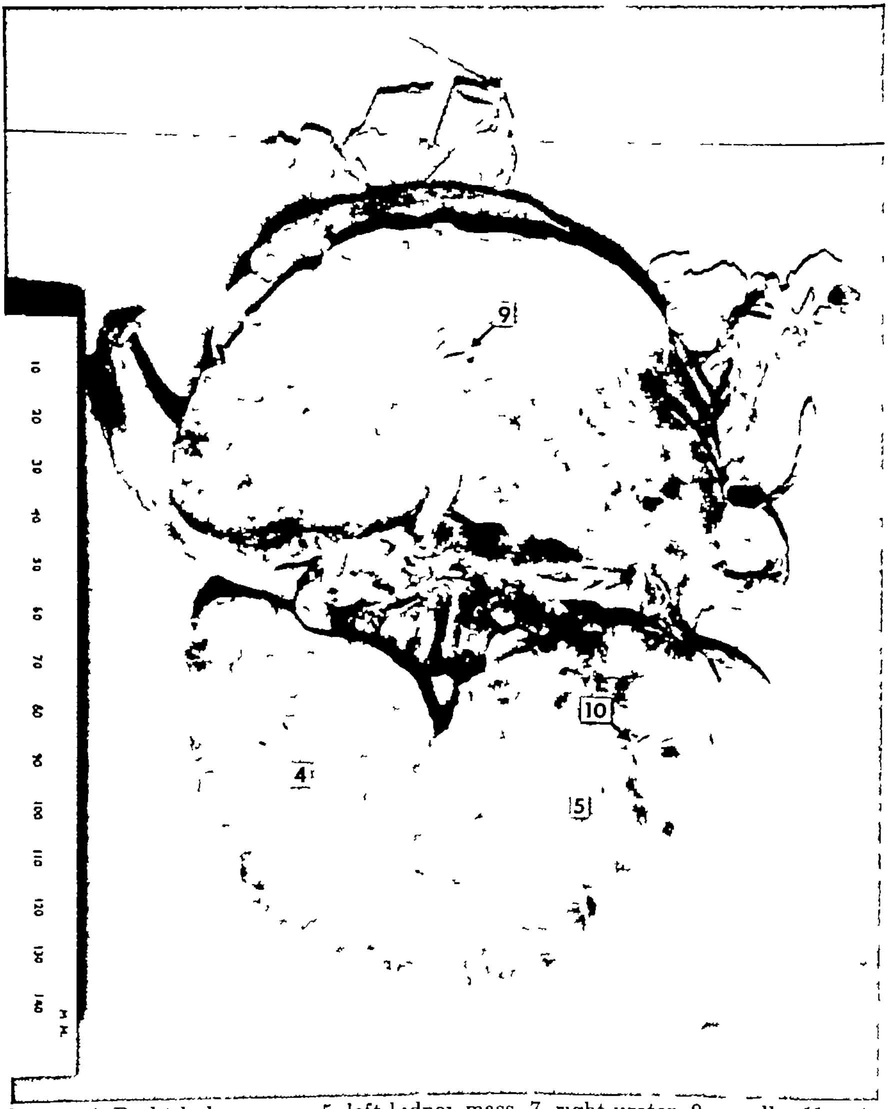

Fig 3 4, Right kidney mass, 5, left kidney mass, 7, right ureter, 9, papilla, 11, artery, 12, pyramid

it was in relation to the iliacus and the psoas muscles Medially it extended to the midline of the vertebral column The left adrenal gland was somewhat flattened, but was situated in about the normal position The right adrenal gland could not be found There was a large mass of perirenal fat surrounding the kidney

Grossly this kidney resembles the classical "cake" kidney It measures 10 5 cm at its greatest diameter and weighs 260 gm The anterior surface is lobulated and shows some semblance of a hilum in the region which probably represents the right kidney The posterior surface (fig 1) is smooth and concave with but very slight lobulation Some division into right and left parts can be seen externally

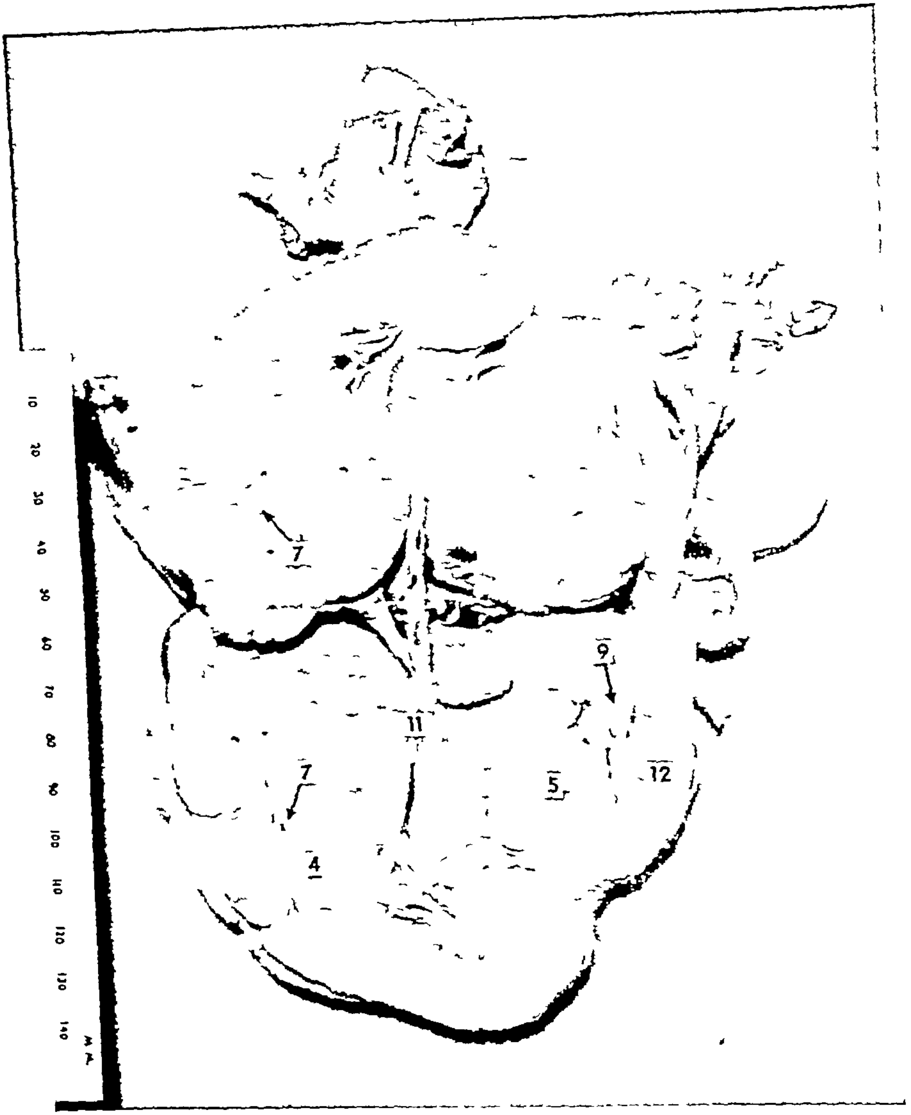

FIG 4 4 Right kidney mass, 5 left kidney mass, 9, papilla, 10 calyx like structure

from the anterior aspect (fig 2) Sections were made to ascertain the degree of division present (figs 3, 4, 5) Anteriorly the sections show rather good demarcation, but in the posterior region this demarcation begins to fail

The ureters were well formed and entered the bladder in the normal relationship The left ureter had origin from five external calyces These calyces arose from a rather large area of the anterior surface of the left portion of the kidney mass The right ureter had origin from four external calyces in a hilum-like formation extending the entire length of the anterior surface of the right portion of the kidney The branches of the right and left ureters are derived rather distinctly

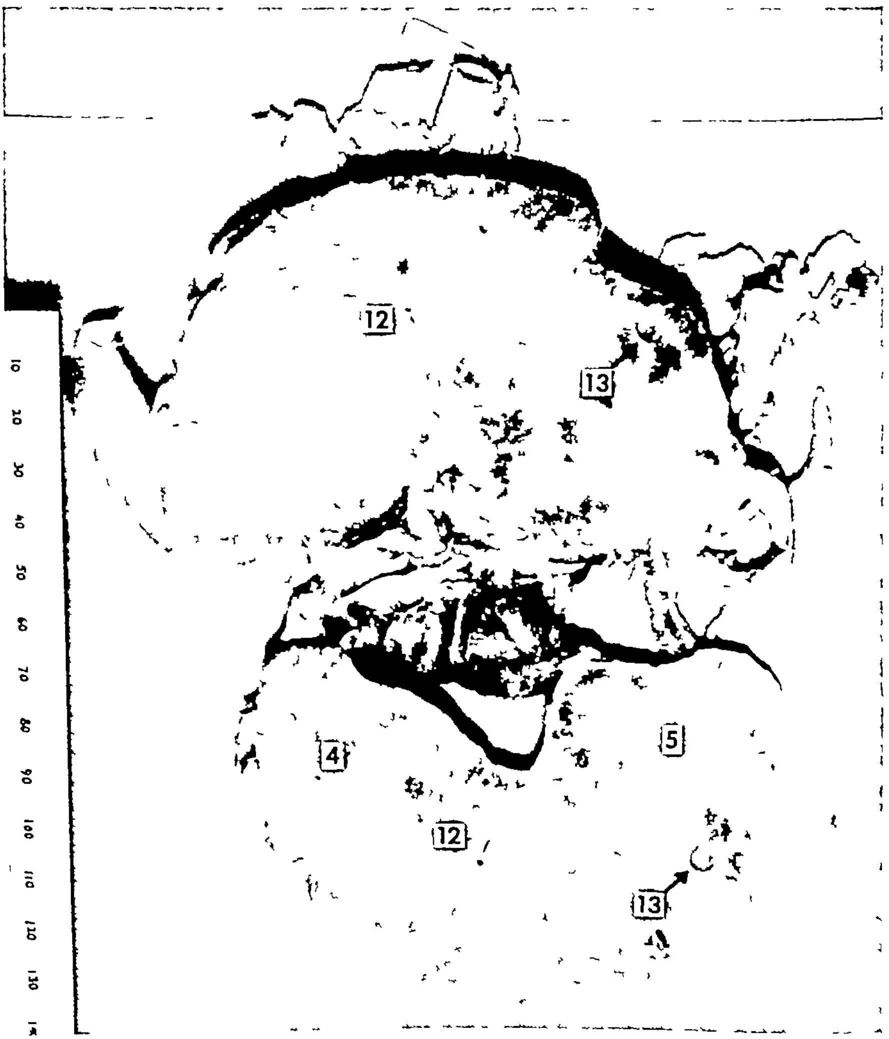

FIG 5 4, Right kidney mass, 5, left kidney mass, 12, pyramid, 13, cyst

from the respective right and left portions of the kidney These facts were ascertained by the study of sections

The arterial supply was derived from the abdominal aorta near the bifurcation The right artery arose from the proximal portion of the right common iliac artery and divided into two large branches, both going to the right portion of the kidney One branch entered the smooth posterior surface and the other branch entered the hilum-like formation The left artery arose at the bifurcation of the aorta and was distributed largely to the left portion of the kidney with one fairly large branch going to the right portion The venous drainage showed less division into the right and left parts than did the arterial supply One large vein

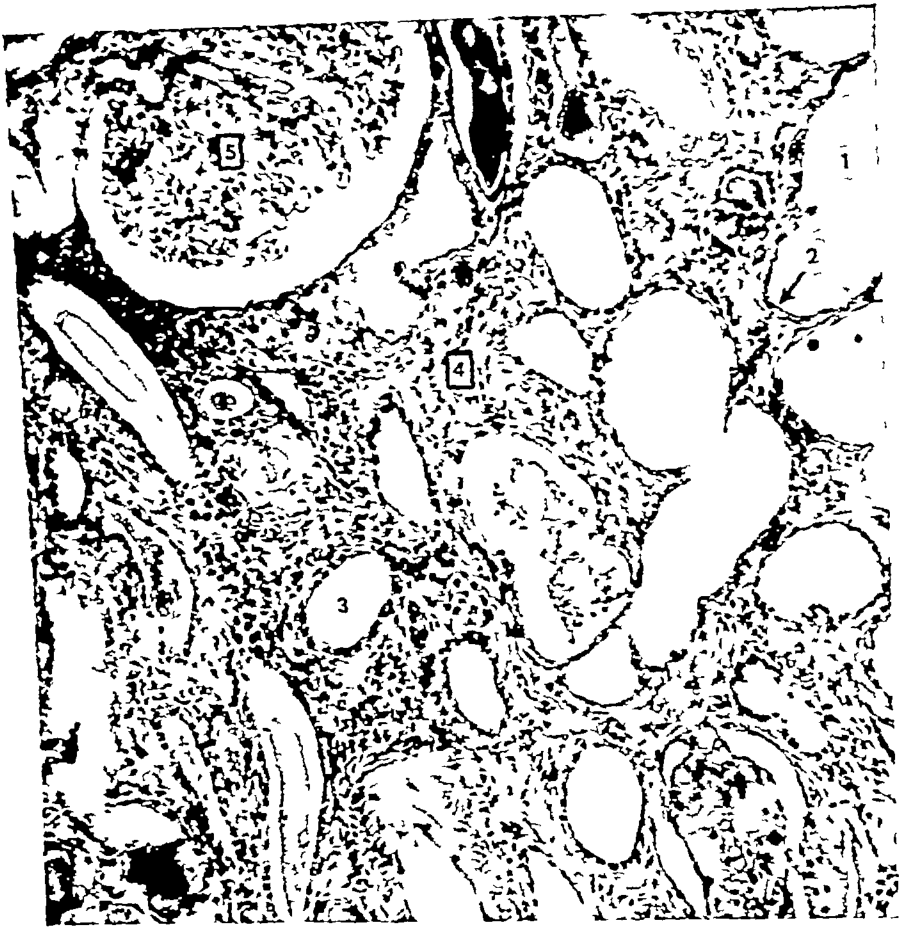

FIG 6 1, Serous cyst, 2 flattened epithelium, 3, enlarged tubules, 4, excessive interstitial connective tissue, 5, glomerulus

arose from the entire anterior surface of the kidney and entered the inferior vena cava about 4 cm above the bifurcation A smaller vein arose on the most medial aspect of the kidney and entered the proximal part of the left common iliac vein

Genesis of this type of kidney is further mirrored by the characteristic fetal lobulation, which is relatively common (fig 1) in arrested development, however, function is apparently adequate Kidney cysts are of three principal types and can be either mixed or of a specific type such as solitary cysts which are large and individual by nature, retention cysts due to renal vascular or inflammatory disease resulting in tubular dilatation or congenital polycystic kidneys Solitary cysts may be hemorrhagic but in this instance contained serous fluid They varied considerably in size and were either congenital in origin or were the result of tubular obstruction

The congenital polycystic kidney is a genetic maldevelopment Insufficient functioning renal tissue may result in early death In this instance adequate renal tissue was present, and little or no clinical evidence of maldevelopment appeared until about the 35–45th year of life At this time renal failure resulted from progressive increase in the size and/or number of cysts (figs 5 and 6)

Renal enlargement is usually due to increase in size of individual cysts, rather than to increase in number The cake kidney has a follicular or irregular profile The cysts are lined by low cuboidal or flattened epithelium (fig 6) The remaining renal tissue is hypoplastic, the number of nephrons apparently being reduced due to excessive interstitial connective tissue

This renal malformation is a result of faulty embryogenesis The kidney is developed from two separate portions which must unite One portion, from metanephric blastema, forms convoluted tubules and glomeruli The other portion, from the wolffian duct, forms ureter, renal pelvis, and collecting tubules Faulty embryogenesis of collecting ducts with convoluted tubules tends to give rise to the cystic change

SUMMARY

The tenth example of a fused pelvic (cake) kidney is reported with a comprehensive review of pertinent literature These cake kidneys are unique in their lack of symmetry and in their fetal characteristics The unusual gross vascular and excretory components are described and illustrated The histopathology is reviewed and illustrated

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ECHINOCOCCUS DISEASE OF KIDNEY: REPORT OF A CASE

WILLIAM L. HUFFMAN

Typically the areas of echinococcus infestation are the sheep and cattle raising districts of the world, as for example South America, Australia, New Zealand, South Africa, Asia, Central and North Europe and the countries within Asia and Africa bordering the Mediterranean. At one time the incidence in Iceland was extremely high but this has been decreased markedly in recent years with proper public health measures. By 1940, 519 cases had been reported in the American literature, 95 per cent of which were in immigrants.

The parasite causing the disease is the Echinococcus granulosus. It measures from 2.5 to 9 mm. in length and consists of three parts: a head or scolex, neck and three tail segments or proglottids. The scolex contains a rostellum with a double row of hooklets and four suckers which facilitate attachment to the intestinal mucosa.

The definitive hosts are dogs, also wolves, jackals and coyotes. Intermediate hosts are man, cattle, sheep, horses, hogs and other herbivorous animals. Ova evaculated in the feces are ingested by man or other intermediate hosts. In the duodenum the embryo escapes from the embryophore and attaches itself to the intestinal mucosa which is penetrated with entrance into mesenteric veins or lymphatics. The ova then may pass to various parts of the body, most frequently entering the portal system and lodging in the liver. If not destroyed by phagocytic cells the hooklets disappear, the larva undergoes central vesiculation and the cyst begins to increase in size. Formation of a cyst within the kidney presupposes passage through the portal system and also through the pulmonary circulation unless a patent foramen ovale is present. Renal hydatid is uncommon and comprises about 2.5 per cent of all cases of infestation.

As the cyst grows the enveloping membrane becomes differentiated into an external laminated layer and an internal germinal layer. Within the cyst cavity are found fluid, brood capsules, scolices and daughter cysts. The daughter cysts arise from the germinal epithelium of the primary cyst wall and also from brood capsules and scolices. When a brood capsule ruptures the scolices escape into the hydatid fluid and are known as hydatid sand. Infection usually takes place during childhood but does not become clinically manifest until adult life.

The symptoms of renal hydatid may be only vague pain in epigastrium or flank, varying degrees of discomfort on urination, or when there is communication between the cyst lumen and the renal pelvis there may be renal colic due to passage of hydatid sand, small daughter cysts or shreds of the enveloping membrane.

The diagnosis can be made by a clinical awareness of its incidence in patients living in or coming from areas where the disease is prevalent and in whom urinary symptoms and radiographic findings are suggestive. The cyst wall may

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Read at annual meeting North Central Section of American Urological Association, Cleveland, Ohio, October 3-5, 1956.

occasionally undergo calcification which can easily be seen on the x-ray film The diagnosis becomes obvious when formed cyst material is passed in the urine Two tests for hydatid sensitivity can be performed, the intradermal test is the most sensitive and most widely used After successful operation this test remains positive because of the persistence of fixed antibodies The antibody titre is measured by the complement fixation test, the titre of which falls after surgery and which therefore can be used as a measure of operative success Because of the scarcity of fresh antigen in this country both these testing materials may be difficult to obtain

Operative treatment in the past has consisted of nephrectomy, partial nephrectomy or enucleation of the cyst and marsupialization During any of these operative procedures care must be taken to avoid spillage of the cyst contents since this may cause a severe allergic reaction

CASE REPORT

A S , a 47-year-old Italian man who had recently immigrated to this country, was first seen September 8, 1955 He was referred by his family physician who first saw the patient 3 weeks previously because of intermittent dysuria, frequency and pyuria He complained of vague urinary discomfort for several years, particularly mild dysuria He never had any colicky pain although he had epigastric and right upper quadrant discomfort occasionally He had received sulfa drugs and a broad-spectrum antibiotic which did not alleviate the symptoms and to which the pyuria had failed to respond Four years previously he underwent an uneventful appendectomy

The patient was well developed and well nourished Blood pressure 140/80, pulse 90, respiration 22, temperature 37 6 Mild right costovertebral angle tenderness was present No abdominal masses were palpable Urinalysis specific gravity 1 020, albumin 3 plus, sugar negative, pH 6 0, urine sediment loaded with white blood cells Urine culture showed no growth Blood studies showed hemoglobin 12 mg , white blood cells 14,200, with a differential showing eosinophils 11 per cent in an otherwise normal smear Repeat differential smears showed eosinophils 8 per cent and 9 per cent Intravenous pyelograms showed a normal and satisfactorily visualized left upper urinary tract On the right side the visualization was unsatisfactory (fig 1, *A*) There was excretion of contrast medium in what appeared to be dilated calyces at the lower pole with the possibility of a tumor mass at the upper pole At cystoscopy the bladder mucosa was found to be mildly inflamed Both ureteral orifices were normal in size and position Urinalysis again showed many white blood cells and red blood cells and urine culture was negative Urine from the left kidney was clear and negative microscopically That from the right contained many white blood cells No abnormal constituents could be identified A retrograde pyelogram of the right kidney showed compression and elongation of the calyces due to an upper pole mass that was well outlined (fig 1, *B*) The epithelial lining of the pelvis and upper ureter appeared to be ragged No antigenic material for skin tests or complement-fixation study could be obtained

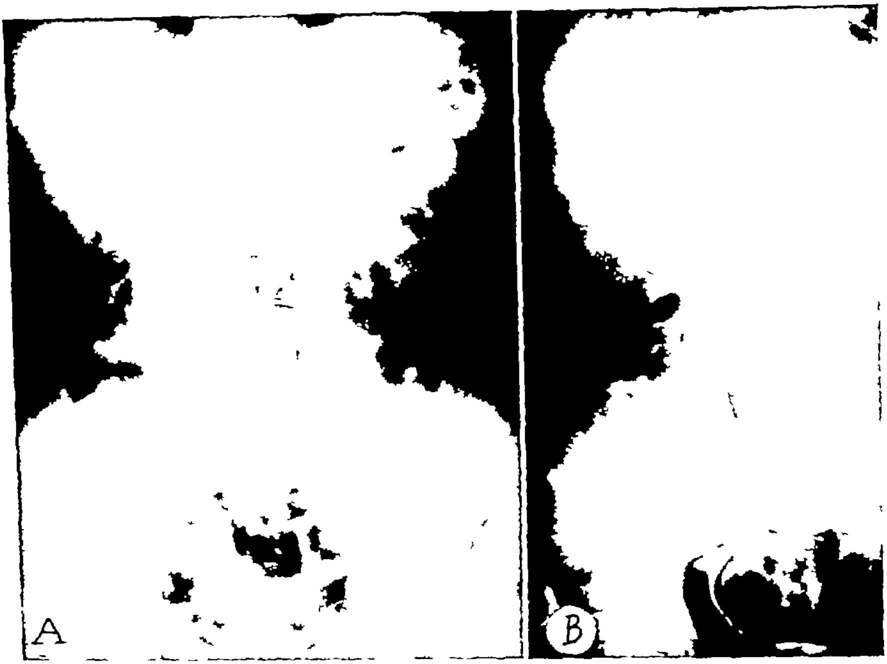

Fig 1

Right renal exploration was performed with a preoperative diagnosis of probable echinococcus cyst of right kidney Incision was made over the twelfth rib which was resected subperiosteally Examination showed the kidney to be enlarged It was extremely adherent to the adjacent perirenal fat and there was a large tumor mass at the upper pole with dense adherence to the peritoneum underlying the lower border of the liver The ureter was found to be markedly thickened A right nephrectomy was performed The patient's postoperative course was uneventful He now has no urinary symptoms and the urinalysis is negative

Pathological report (William Sinclair Jr , M D) ' The gross specimen consists of a previously sectioned fluctuant cystic mass resembling kidney measuring 12 by 8 by 7 5 cm in greatest dimensions (fig 2) Transections show the cortex and medulla to be markedly thin The cortex ranges from 0 1 to 0 5 cm in thickness and the medulla consists only of a thin firm membranous structure The pelvis and major and minor calyces are dilated empty and distorted by a cystic mass lined by opaque gray membranous tissue The mass measures 7 by 8 by 6 cm in greatest dimension and contains numerous similar thin-walled cysts ranging from 0 1 to 3 5 cm in greatest dimension These cysts contain clear fluid in which are abundant minute gray particles Attached to the kidney is a segment of ureter measuring 7 cm in length and 2 cm in diameter '

Microscopic study Material from the small cysts was placed on a glass slide and examined without stain and disclosed numerous scolices with hooklets typical of Echinococcus granulosus in the larval phase (fig 3) occasionally undergo calcification which can easily be seen on the x ray film The diagnosis becomes obvious when formed cyst material is passed in the urine Two tests for hydatid sensitivity can be performed, the intradermal test is the most sensitive and most widely used After successful operation this test remains positive because of the persistence of fixed antibodies The antibody titre is measured by the complement fixation test, the titre of which falls after surgery and which therefore can be used as a measure of operative success Because of the scarcity of fresh antigen in this country both these testing materials may be difficult to obtain

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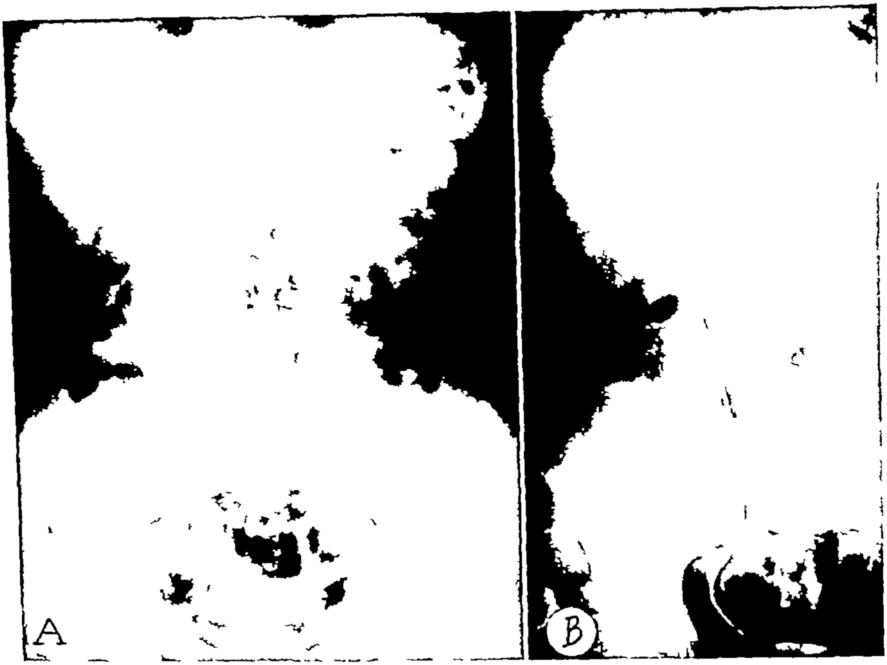

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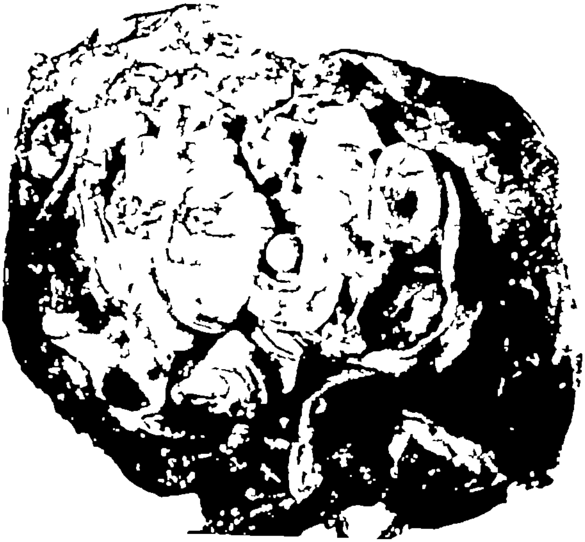

FIG 2

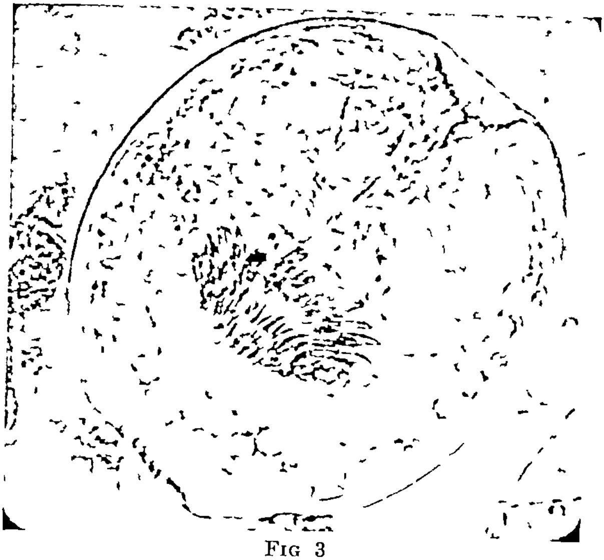

FIG 3

"The cyst wall (primary cyst) is lined by relative acellular pink-staining fibrillar material in which are a few lymphocytes This represents the cuticular or laminated layer In some places the lining is composed of clusters of large cells which are frequently multinucleated and which have poorly defined cell borders and are multilayered Some of these cells may be foreign body giant cells, others probably represent residual germinative or embryonic membrane from which daughter cysts arise The outermost layer is composed of loose fibrous tissue infiltrated with lymphocytes, plasma cells and eosinophils This layer is adherent to the serosa of the pelvis The pelvis shows squamous metaplasia of epithelium and infiltration of the wall with lymphocytes, plasma cells and eosinophils In some places there is amorphous basophilic and eosinophilic debris and adjacent to this, projecting into the lumen of the cyst, are small cysts lined by flattened or cuboidal epithelium

"Section of kidney shows the cortex and medulla to be infiltrated with lymphocytes and plasma cells, with marked atrophy of tubules and glomeruli in some places There is hyperemia and interstitial hemorrhage

"Sections of ureter show a squamous metaplasia and marked chronic inflammation

"Diagnosis Echinococcus cyst of kidney, chronic pyelonephritis, chronic inflammation of ureter"

SUMMARY

The incidence, etiology, diagnosis and treatment of echinococcus disease of the kidney have been briefly outlined A case of renal hydatid disease, diagnosed preoperatively, is reported

301 Republic Bldg , Cleveland 15, Ohio

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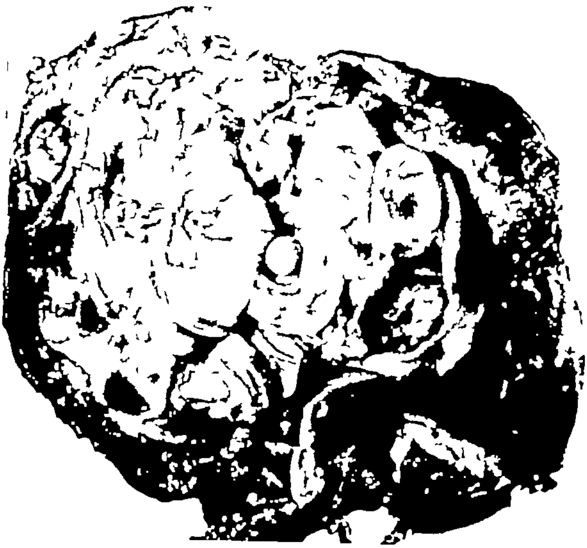

FIG 2

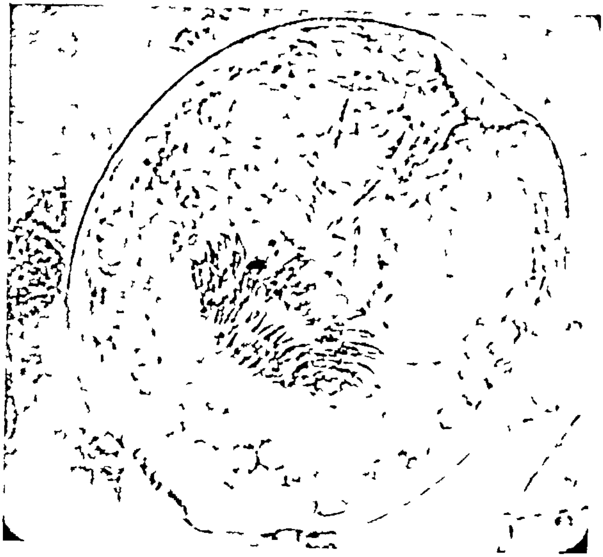

FIG 3

"The cyst wall (primary cyst) is lined by relative acellular pink-staining fibrillar material in which are a few lymphocytes This represents the cuticular or laminated layer In some places the lining is composed of clusters of large cells which are frequently multinucleated and which have poorly defined cell borders and are multilayered Some of these cells may be foreign body giant cells, others probably represent residual germinative or embryonic membrane from which daughter cysts arise The outermost layer is composed of loose fibrous tissue infiltrated with lymphocytes, plasma cells and eosinophils This layer is adherent to the serosa of the pelvis The pelvis shows squamous metaplasia of epithelium and infiltration of the wall with lymphocytes, plasma cells and eosinophils In some places there is amorphous basophilic and eosinophilic debris and adjacent to this, projecting into the lumen of the cyst, are small cysts lined by flattened or cuboidal epithelium

"Section of kidney shows the cortex and medulla to be infiltrated with lymphocytes and plasma cells, with marked atrophy of tubules and glomeruli in some places There is hyperemia and interstitial hemorrhage

"Sections of ureter show a squamous metaplasia and marked chronic inflammation

"Diagnosis Echinococcus cyst of kidney, chronic pyelonephritis, chronic inflammation of ureter "

SUMMARY

The incidence, etiology, diagnosis and treatment of echinococcus disease of the kidney have been briefly outlined A case of renal hydatid disease, diagnosed preoperatively, is reported

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CONGENITAL CYSTIC HYDROCALICOSIS (UNILATERAL MULTICYSTIC DISEASE)

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Recently efforts have been made to elucidate and classify more accurately the anatomical and clinical manifestations of cystic renal diseases Spence[1] and DeWeerd and Simon[2] have reported a study of congenital cystic lesions of the kidney in which they carefully separated multicystic, multilocular cystic, simple cystic and polycystic diseases of the kidney on the basis of anatomic and roentgenographic characteristics and prognosis Spence, describing multicystic disease, stated "The typical clinical picture consists of the finding of a mass in the renal area in an otherwise healthy infant with nonfunction on the excretory urogram on the involved side in association with a normal contralateral kidney " Anatomically, there is a "replacement of normal kidney by a conglomeration of varying sized cysts with no discernible renal parenchyma often associated with absence or atresia of the ureter " This entity is regarded as separate and distinct from polycystic disease and multilocular cysts of the kidney

Although the usual presenting complaint is that of an abdominal mass, we wish to present the case of a child with unilateral multicystic disease in which no renal mass was palpable and whose chief symptom was recurrent transient pyuria This case is significant, however, because of the fact that pathological studies of the surgical specimen have enabled us to re-evaluate the pathogenesis of this complex congenital disorder

CASE REPORT

(C-4379) A 6-month-old male infant was admitted for the third time on June 4, 1956, for re-evaluation of unexplained recurrent fever and failure to gain weight The child had been delivered one month prematurely by planned cesarian section Following birth, he had been cyanotic for 48 hours, during which time oxygen had been administered At 3 months of age, because of the possibility of hydrocephalus, he was hospitalized for study This condition was not found to be present An intravenous pyelogram showed an absent right renal shadow and a normal left kidney Cystoscopy and retrograde pyelography revealed absence of the right ureteral orifice The retrograde pyelogram on the left was normal (fig 1)

On his second admission 1 month later, the diagnosis of craniosynostosis was considered, but disproven The cystoscopic and retrograde pyelographic findings were unchanged The initial urine specimen contained a few clumps of white

Accepted for publication January 21, 1957

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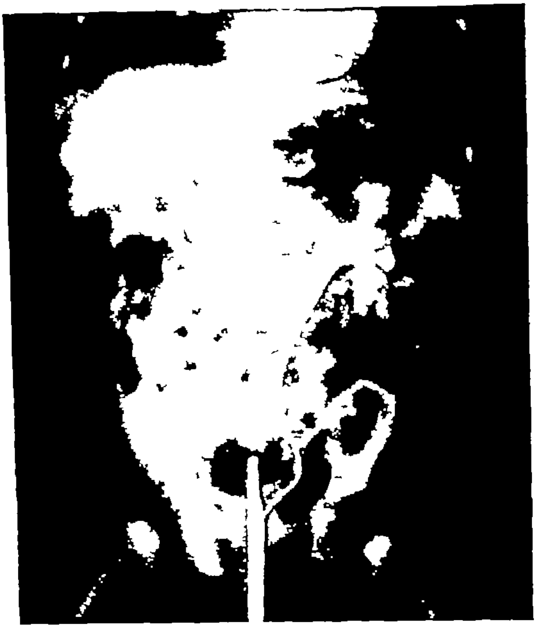

FIG 1 Retrograde pyelogram showing compensatory hypertrophy of left kidney and absent right renal shadow

blood cells although centrifuged specimens at the time of cystoscopy failed to show pyuria The impression of the urologist at that time was probable right renal agenesis

Following discharge, the infant had frequent colds, episodes of fever, and failed to gain weight There were no symptoms referable to the urinary tract The infant was then admitted for the third time because it was felt that there was an underlying urological disorder that required further study The child presented as an undernourished, 14 5 pound, 6-month-old male infant who fell into the Stuart 5 per cent developmental group His temperature was 101F Physical examination was completely negative The urine contained 10 white blood cells per high power field with an occasional clump of pus cells The results of additional laboratory investigations revealed hemoglobin of 9 9 gm , hematocrit 33 and a white blood cell count of 12,600 The nonprotein nitrogen was 41 mg per cent Streptococcus viridans was isolated from a throat culture and blood culture yielded nonhemolytic gram-positive cocci A urine culture showed gram-negative bacilli of the coliform group

On June 6, 1956, cystoscopy was again performed A careful search was made for an ectopic ureteral orifice, but none was found However, at the site where the right ureteral orifice would normally be situated, there was an apparent small blind cellule, impenetrable to catheters and resistant to retrograde introduction of dye Centrifuged urine specimens obtained at cystoscopy were negative for pus cells and a specimen obtained the next day contained only an occasional white blood cell In view of the negative cystoscopic findings, absence of pyuria during three urologic examinations and an absent right renal shadow,

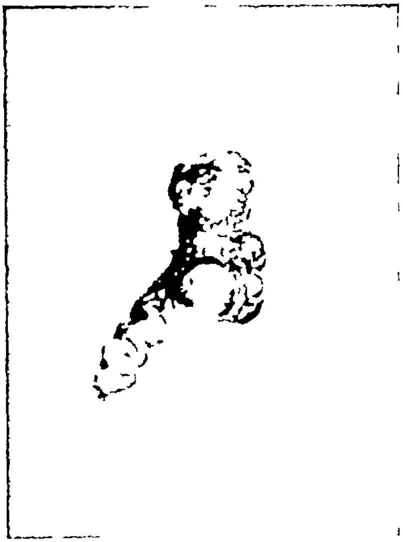

FIG 2 Surgical specimen showing dilated cysts (minor calyces) attached to redundant hydroureter terminating in an atrophic cord

the urological consultant felt that right renal agenesis was still the most tenable diagnosis However, it was decided to perform a flank exploration

Upon entering the right retroperitoneal space, a number of firm, nodular structures suggesting scybala were palpated along the ascending colon However, after difficult dissection, about eight small connected cysts, appearing much like discrete marbles, were separated from the posterior parietal peritoneum These cysts were attached to a dilated redundant ureter which was distended and tense with urine As it approached the bladder, the ureter became a filamentous cord (fig 2) No grossly recognizable renal tissue could be found and nephro-ureterectomy was performed, ligating a hypoplastic renal pedicle Gross examination of the operative specimen revealed a pinhole opening at the end of the aplastic ureter which ejected a tiny drop of purulent urine on compression of the proximal cysts

The specimen consisted of a lobulated cluster of 10 to 15 cysts measuring approximately 5 5 by 2 by 2 5 cm , in continuity with a 5 cm long segment of ureter Each cyst varied in size from 1 5 to 2 5 cm in diameter No recognizable renal tissue was present The external surface was smooth and gray-white and, on opening, each cyst was filled with thin, straw-colored fluid The lining was smooth No grossly recognizable renal tissue could be found in the walls of the cysts or between them The pelvis and proximal portion of the ureter were dilated and thin-walled and the mucosa was smooth, shiny and pinkish gray At the distal end of the ureteral segment the wall was thickened and the lumen markedly stenosed

Histologically, each cyst had an imperfectly layered fibromuscular wall, in the fibrous stroma of which were some evidences of attempts to form abortive

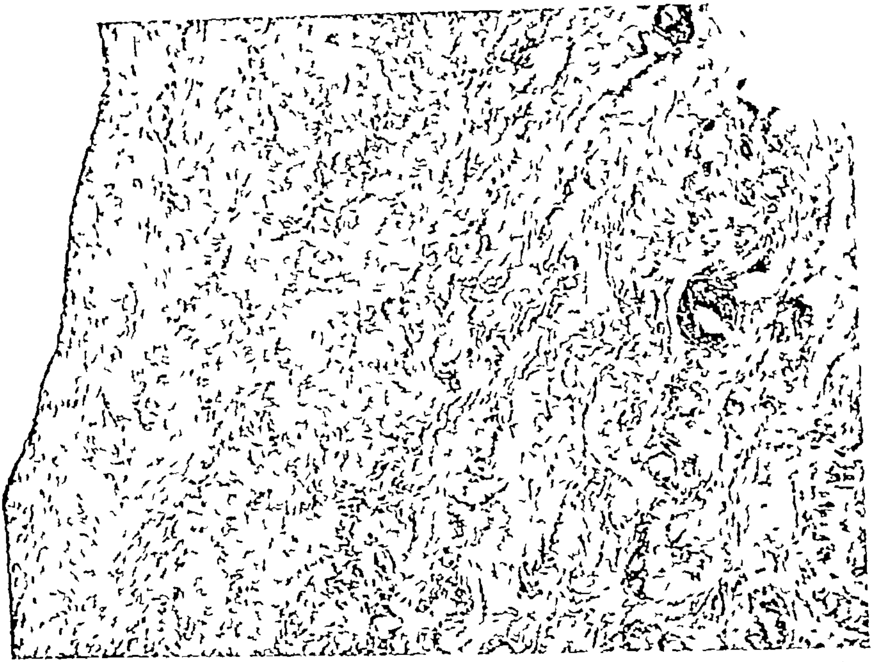

FIG 3 Wall of renal cyst showing the presence of layers of muscle and minute tubules × 130

renal tubules or imperfect glomeruli (fig 3) Special stains to demonstrate muscle and connective tissue clearly showed the presence of these tissues, thus indicating that the walls of the cysts were structurally similar to the walls of normal calyces

DISCUSSION

Embryologically, the ureter, a derivative of the wolffian duct, having taken its origin as a bud from the cloaca, grows cephalad It may, for reasons thus far unknown (possible first trimester infections, etc), become arrested in its linear progress at any stage, giving rise to a defect that may vary from a blind trigonal dimple to an elongated, superiorly closed, sac-like structure It may be normal in caliber or merely an atrophic cord, especially in its upper portion which is the last to mature

However, once the ureter reaches the mesodermal mass of nephrogenic tissue, it initiates renal differentiation Fairly well established is the theory that the metanephric renal anlage will not develop glomeruli or convoluted tubules until contact is made with the ascending primitive ureter Now the ascended ureter, in juxtaposition with the blastemic mass, is either capped by this tissue or penetrates it Meanwhile, the collecting tubules develop from the ureteral bud and stimulate the mesodermal nephrogenic mass to form convoluted tubules and glomeruli Rudimentary metanephic tissue, when it is found in a renal fossa area, is often classed as unilateral renal agenesis However, this type of defect

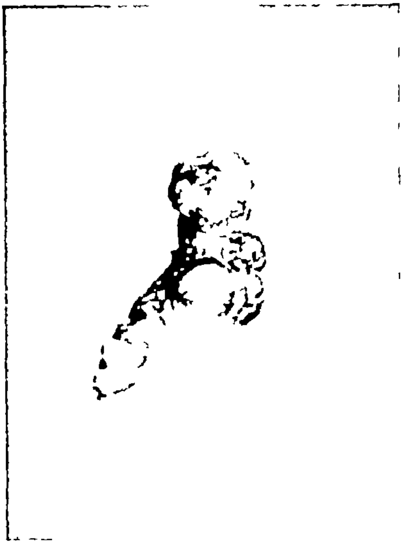

Fig. 2. Surgical specimen showing dilated cysts (minor calyces) attached to redundant hydroureter terminating in an atrophic cord.

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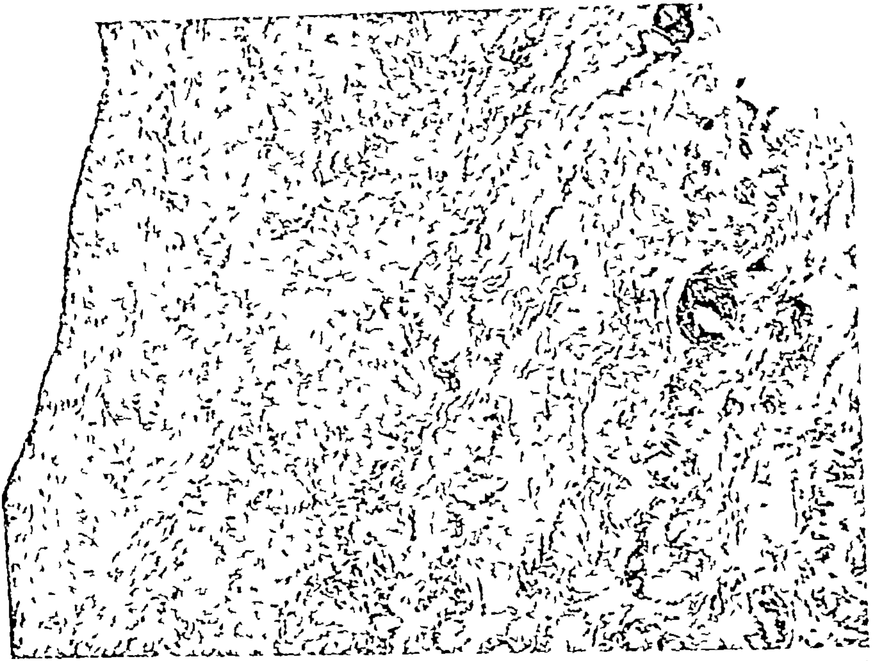

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Although unilateral multicystic lesions of the type here described are grossly characterized by a cluster of cysts without discernible renal parenchyma, histologic study of this malformation usually reveals the presence of abortive tubules and glomeruli These findings are evidence of imperfect differentiation of the mesodermal nephrogenic mass and indicate the presence of the ureteral bud stimulus Thus this entity must be considered to be a form of renal hypoplasia

The striking feature of this group of hypoplastic kidneys is the presence of gross discrete cysts of variable size, usually 10 to 20, a number significantly approximating the normal number of minor calyces Another gross characteristic is the constant association with some degree of ureteral stenosis capable of causing proximal dilatation We believe that these cysts arise as the result of congenital ureteral obstructive hydrocalicosis, probably developing in the 10 mm stage embryo The "blunted" calyceal buds imperfectly enter the mesodermal mass and fail to induce normal differentiation Twenty years ago, Schwartz when first employing the expression, unilateral multicystic disease similarly left it plausible that this renal anomaly had its origin at any early stage in the developmental process [4] Although Spence stated that this condition can in no way be considered a hydronephrotic phenomenon, he acknowledged that in some instances there is communication between the cysts and the ureter Furthermore, he illustrated the entry of dye via a stenotic ureter into cysts in a roentgenogram of the specimen from his first case Goodyear and Beard, in addition, noted in two case reports the communication of some cysts with the pelvis by a small orifice and felt that an underlying congenital ureteral obstruction might be responsible for this renal defect [5] It is our feeling that this complex abnormality is actually the result of partial to complete failure of union of the primitive ureter and the nephrogenic blastema as a result of hydrocalicosis caused by proximal ureteral obstruction Thus, the "grapes on a stem" seen surgically are nothing more than dilated calyces capable of communicating with the pelvis, becoming secondarily infected, and discharging purulent urine An alternative, more descriptive terminology, which would indicate the pathogenesis of this entity, would be "congenital cystic hydrocalicosis" Anatomical support for this concept is the demonstration of one or more layers of muscle in the walls of these cysts, for normally muscle is found in the kidney only in relation to the calyceal fornices

This cystic, hypoplastic malformation becomes evident as a unilateral, noninherited, nonprogressive, congenital condition In 16 of the 19 previously reported cases, there was a palpable flank mass as the presenting complaint However, the size of the renal mass is governed by the site of the ureteral stenosis For example, lower ureteral stenosis in the fetus would lead to an earlier dilatation of the proximal ureter and lesser degrees of hydrocalicosis In the majority of the previously reported cases the stenosis has usually been in the upper ureter which would facilitate the development of earlier greater more readily palpable calyceal cysts Our case of lower ureteral obstruction, caused an initially greater ureteral distention with relatively small calyceal cysts and clinically a nonpalpable kidney and a radiologically absent renal shadow The atretic portion of ureter may have a pinhole size lumen impenetrable to diagnostic aids, but readily capable of transmitting pus cells intermittently or continuously from an infected renal cyst, as demonstrated in our case

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[3] Bell, E T Renal Diseases Philadelphia Lea and Febiger, 1946, p 58

[4] Schwartz, J An unusual unilateral multicystic kidney in an infant J Urol, 35 259–263, 1936

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In two of the previously reported cases, there were concentric renal calcifications, and these examples, coupled with those of the palpable kidney made surgical exploration mandatory for presumptive neoplasm Engel[6] recently stressed the need for exploration in the presence of minimal signs for nonfunctioning halves of double kidneys Apparent renal agenesis with constitutional signs of infection and no consistent urological signs or symptoms as in our case, should also be considered an indication for flank exploration, particularly in the pediatric age group

SUMMARY

A case of congenital cystic hydrocalicosis (unilateral multicystic disease) with the primary symptoms of recurrent fever, failure to gain weight transient pyuria and no palpable renal mass is presented

The microscopic demonstration of the abortive development of tubules and or glomeruli indicates that this condition must be considered an extreme form of renal hypoplasia

The presence of muscle in the walls of these renal cysts and their gross number suggested that they are embryologically imperfectly formed minor calyces

The site of ureteral obstruction determined the degree of renal cystic enlargement and the presence or absence of a clinically palpable mass It is suggested that a more descriptive alternative term for unilateral multicystic disease be congenital cystic hydrocalicosis

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[6] Engel, W J Remarks from case presentations, at A U A meeting, Boston, 1956

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INFLUENCE OF SEX HORMONES ON FORMATION OF EXPERIMENTAL VESICAL CALCULI IN MALE RATS

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In humans, the incidence of urinary lithiasis is significantly greater in males than in females [1 4] See table 1

It is generally accepted by most investigators that the male dominance in urolithiasis is attributable to the close proximity of the genital and urinary tracts This proximity predisposes to obstruction and stasis It has been shown that urinary tract infection[5 7] is an important enhancing factor in the genesis of urinary calculi The relatively longer male urethra and the prostate (especially in the presence of enlargement of this gland) make it more difficult for the male to pass small stones This is the common anatomical explanation of sex incidence of calculi favoring the male

Although there is a good deal written on the anatomic predisposition to stone formation in the male, other mechanisms may be involved Butt[4] points out that women are more prone to upper urinary tract infection than men, yet, as shown by Lett, Higgins and Winsbury-White in their individual series (table 1), lithiasis is more common in males than in females Randall,[8] on papillary calcification covering 239 necropsies, found calcium plaques to be about twice as common in the male as in the female On an experimental basis, Marshall and associates[9] demonstrated a consistent sex difference in the Wistar rat under varied conditions In those implanted with human stone fragments, the average weight of the stones increased 220 per cent in the male, but decreased 90 per cent in the females Another implanted group of both sexes treated with hyaluronidase showed the same marked sex difference When the results of this experiment were compared with those of the previous one, no effect of the hyaluronidase was noted Etherization enhanced stone formation, but, in addition, there was a proportionately greater response in the males than in the females Gershon-

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TABLE 1 *Summary of clinical statistics on urolithiasis showing male dominance*

Series	Total Number of Cases	Sex Incidence		Sex Ratio Males/Females
		Males	Females	
Butt[4]	185	121	64	1 9
Higgins[2]	857	677	180	3 8
Winsbury-White[1]	866	589	277	2 1
London Hospital[1]	2574	1660	914	1 8
Lett[3]	2708	1760	948	1 9
Total	7190	4807	2303	2 1

Cohen and others[10] produced stones in 14 out of 46 female Wistar rats within 15 to 60 weeks with 1 mg testosterone propionate 3 times weekly Twenty male rats given the same treatment, and litter-sister controls receiving no treatment formed no stones Work of the above observers may implicate a heretofore unrecognized reason for the sex difference other than the anatomical differences in the genitourinary systems in the two sexes

Two other mechanisms affecting stone formation involving sex hormones have been studied In a series of 462 studies on protective urinary colloids, Butt[4] demonstrated that women have more protective activity than men, pregnant women, more than nonpregnant women, and Negros (both sexes) have the highest degree of protective colloidal activity He found only 8 cases of urolithiasis in 13,000 pregnancies, whereas 23 out of 64 female stone formers were nulliparous A second mechanism which links citrate excretion, sex hormones and calcium solubility and excretion was uncovered by Shorr and others [11] [12] They demonstrated that injected estrogens increased citrate ion excretion The citrate ion combined with calcium, forming a soluble calcium-citrate complex, thus decreasing the concentration of free calcium ions available for crystallization with phosphates Cyclic alteration of citrate excretion during different phases of the menstrual cycle was established, viz, low excretion during menstruation, with higher output about the middle of the cycle They administered estradiol benzoate to two amenorrheic girls, causing significant increase in citrate excretion during treatment, with a sharp return to lower levels on its discontinuance A male with pituitary hypogonadism showed a decrease in citrate excretion during testosterone treatment, with an increase when the hormone was discontinued Scott and others[13] in working with blood and urinary citrate tolerance levels in normal people and in stone formers, found that *greater amounts* of citric acid were excreted in the urine of normal adults, beginning at puberty, than in children, debilitated persons and aged men Sex differences were not mentioned Thus, sex hormones may play a more important role than previously

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TABLE 2 *Incidence and size of stones formed in Long Evans male rats subjected to endocrine manipulation In the two experiments, changes are similar, but not identical*

Status	Number of Animals	Calculus Incidence	Average Wt Calculus	Per Cent of Control
		%	mg	
1 Intact				
Run 1	42	100	182	
Run 2	18	100	213	
2 Intact-stilbestrol				
Run 2	16	100	172	80
3 Castrate				
Run 1	15	80	135	74
Run 2	18	100	139	65
4 Castrate stilbestrol				
Run 1	11	73	71	39
Run 2	17	100	107	50

believed in the explanation of male dominance in urolithiasis, whether by one or a combination of the above mechanisms, or by other metabolic effects

In previous papers[14] [15] we have shown that the pituitary hormones and androgens play an important contributing role in experimental calculogenesis In intact female rats, the incidence and size of calculi were much smaller than in males By removing the ovaries and treating with testosterone, but not with either alone, the incidence and size were increased to male levels The present study shows the effect of sex hormones on calculogenesis in male rats

MATERIALS AND METHODS

Cylindrical C P magnesium niduses were aseptically implanted into the bladders of Long-Evans male rats by Vermeulen's method [16] In certain groups, a bilateral orchiectomy was performed simultaneously Groups of 20 animals were treated as follows untreated controls, intact, treated with 10 micrograms of stilbestrol in corn oil daily, castrate and castrate-stilbestrol treated For each group, five additional animals which did not carry magnesium niduses, but which received the same endocrine treatment, were used for urine collections and as controls Animals were fed Purina Laboratory Chow and water ad libitum Three to five 24-hour urine collections were made for each rat Urinary magnesium, calcium and phosphorus were determined only on specimens from rats not implanted with niduses The quantitative methods employed were those of Denis,[17] Terri[18] and Fiske and Subbarow,[19] respectively At the end of 6 weeks,

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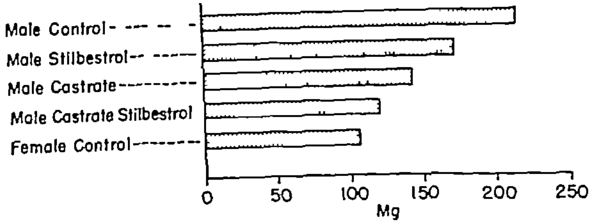

FIG 1 Average size of bladder calculi formed about magnesium niduses in rats subjected to several endocrine plans, experiment 2

TABLE 3 *Urine volume and electrolyte excretion in experiment 2 expressed in ml or mg per 24 hours*

	Urine Volume	Phosphate	Calcium	Magnesium
Intact males	8 8	13 2	14	93
Males—stilbestrol	4 8	7 3	08	88
Castrate males	7 6	11 9	10	1 70
Castrate males—stilbestrol	8 8	10 0	14	97
Intact females	9 0	6 9	19	1 00

the animals were sacrificed The calculi were removed from the bladder, blotted and weighed Animals whose urinary pH exceeded 7 0 were considered infected and were excluded from the final tabulations

RESULTS

No calculi were found in the bladders of rats who were not implanted with magnesium niduses In all intact, untreated animals bearing niduses, calculi were found Calculi formed at the average rate of 0 5 mg per day The incidence of urinary infection was less than 5 per cent Table 2 shows that the best protection against stone formation was afforded by castration and stilbestrol therapy In both experiments, the results were similar In experiment 1, they were more dramatic with a greater decrease in average stone weight and absence of stone in 20 and 27 per cent of animals in groups 3 and 4, respectively In untreated female controls in parallel with these experiments, the incidence was 87 per cent and the average weight, 107 mg The results in experiment 2 are depicted graphically in figure 1 The average size of calculi formed in castrate male rats treated with stilbestrol was almost identical to those formed in intact females Table 3 shows that the excretion of calcium and phosphate and the urine volume were reduced by stilbestrol administration in intact male rats In castrate rats, there was a considerable increase in magnesium excretion When castrate animals were treated with stilbestrol, urinary electrolytes and volume were almost identical to the untreated controls except for slightly reduced phosphate excretion

DISCUSSION

In a previous communication,[15] we have reported that the administration of testosterone to hypophysectomized male rats promoted stone formation In these animals, calcium excretion was slightly reduced, but magnesium excretion was doubled In the present study, castration was found to reduce the size of calculi produced, but the observed changes in electrolyte excretion were almost identical in direction and magnitude Stones formed in stilbestrol-treated intact males averaged 80 per cent of controls They were probably larger than they should have been because of decreased urinary output All animals in this group showed a consistent low urinary volume, but no recognizable edema The effect of urinary concentration was offset by the reduced calcium and phosphate excretion, which may explain the reduced average size of calculi over controls In stilbestrol-treated castrate male rats, the excretion of calcium and magnesium and the urine volume were the same as for controls The phosphate excretion was slightly reduced The mechanism for the reduced stone size is not explained by the *urinary calcium, magnesium and phosphorus excretion* Shorr[11] has indicated that citrate excretion is high in hypogonadal males and is increased in hypo-ovarian women by estrogen administration It is possible that the results in the present study were due to changes in citrate excretion It may be that the excretion of other solubilizing agents such as the urinary colloids was altered by the endocrine manipulations employed

Although the present study may contribute to our knowledge of how stones grow, it does not seem logical to make inferences as to why they form spontaneously, or how they can be dissolved

SUMMARY

Experimental urinary calculi form more readily and are larger in intact male animals than in females Measures directed toward feminizing the male animals decreased the average size of calculi to female levels In order of increasing efficiency in decreasing stone size, these measures were administration of stilbestrol, castration, and castration plus stilbestrol treatment

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MALACOPLAKIA REPORT OF CASE, REVIEW OF LITERATURE

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Malacoplakia, a term introduced in 1903 by von Hansemann, means soft plaque(s) It is essentially a granuloma and is important as a clinical and pathological problem involving differential diagnosis from tumor The plaques appear as discrete, slightly raised, pinkish-brown lesions ranging from 0 1 mm to 3 cm and even larger, particularly when confluent They may show central ulceration and circumferential hyperemia The thickenings are composed principally of histiocytes, called Hansemann cells, and of collections of lymphocytes The large phagocytic cells frequently contain concretions of calcium known as calcospherites or inclusion bodies of Michaelis-Gutmann The calcium is well demonstrated with the von Kossa stain (fig 3, *B*) Small amounts of iron have also been found (Redewill) The lesions are most numerous in the bladder but occasionally involve the ureters and/or pelves In one patient, a girl 6 years of age, the soft plaque was located at the bladder neck, where it acted as a ball valve and caused dilatation of the bladder, ureters and pelves (Morison) The cause and nature of the granuloma are not understood A few have considered the lesion as a neoplastic one (Michaelis and Gutmann, 1902, Michaelis, 1905), the majority have looked upon it as a unique inflammatory process confined to the mucosa (Gierke, Hagmann, Minelli, Pappenheimer, Wegelin, Blum, Rudnick and Ragins, Morison) Some have emphasized the frequent association of an extensive pulmonary tuberculous infection or a profound cachexia in patients with this disease (Michaelis and Gutmann, von Hansemann, Landsteiner and Stoerk, Guterbock, Fraenkel, Kimla, Zangenmeister, Wildbolz, Waldschmidt) but it is maintained by others that this association is coincidental (Gierke, Minelli, Pappenheimer, Panizzoni) In three patients a concomitant Boeck's sarcoid of the skin or lymph node was present (Morison, Hagemann) Monilia were found in the lesions of one of the cases (Dickson, Gray and Kidd) E coli was cultured from the urine of 76 per cent of the cases that have been reported to date (Bleisch and Konikov) Increased permeability of the bladder urothelium to urine or urinary salts, accumulations of blood pigments, and interaction by infecting organisms were some of the factors to which the specific lesion of malacoplakia has been ascribed (Fraenkel, Loele, Opperman) Bodies resembling calcospheroids were produced by incubating blood, broth and urine containing a culture of E coli (Loele) Michaelis-Gutmann-like bodies, have, however, been seen in the mucosa of patients with chronic cystitis but which lacked the plaques of malacoplakia (Wells, Bunting) An histiocytic response is not unusual in any chronic granulomatous cystitis The combination of calcospheroids and histiocytes in characteristic plaque formation is nevertheless unique Because of the greater incidence of this condition in females, a trophic or endocrine factor has therefore

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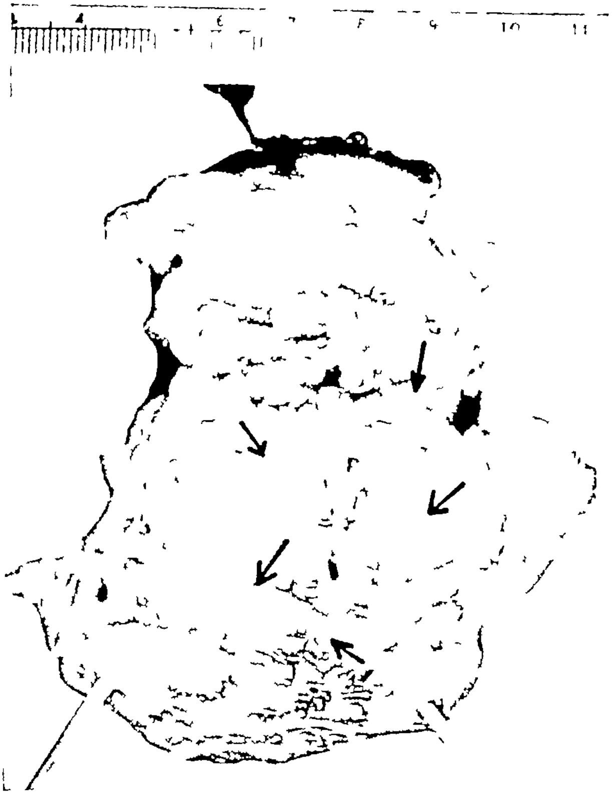

FIG 1 Malacoplakia of urinary bladder, gross specimen Note diffusely spread pale oval, slightly raised areas which appeared pinkish brown when viewed through cystoscope

been suggested (Hagemann, French and Mason) The majority of authors agree that the disease is a granuloma of unknown origin and that it is self-limited

Malacoplakia was present without causing any symptoms, in some it produced painless hematuria but in most of the cases a history suggestive of cystitis was present In one patient a vesical calculus was found (Hagemann), in another a perirenal abscess (McDonald and Sewell) and in two other patients renal calculi were present (Dickson, Gray and Kidd, Hagemann)

There were 54 females and 14 males in 68 case reports (including ours) which were reviewed Thus the condition is considerably more common in females, a ratio of about 4 females to one male The disease can occur at any age, the youngest patients to be reported were 15 months, 6 and 8 years of age (Kaïris, Morison, Opperman), while the oldest were 80 and 96 years old (Guterbock) The greatest incidence was in the age group from 40 to 49 years—about 35 per cent of the patients were in that decade

In the majority of cases, particularly those that were reported before 1920, malacoplakia was an autopsy finding Since 1920 many were discovered at cystoscopy Difficulty in clinical and pathological diagnosis was illustrated by

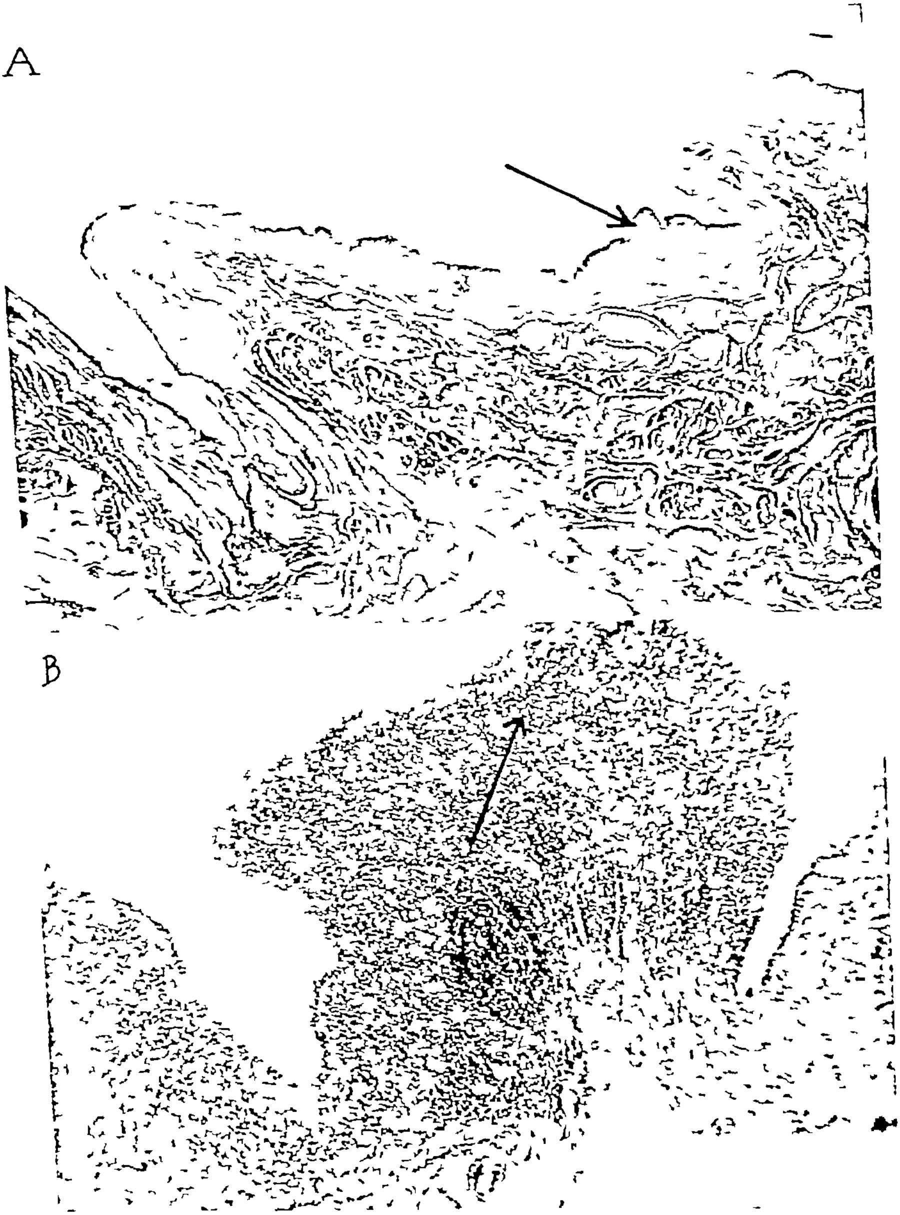

Fig 2 A malacoplakia of urinary bladder Note thickening of submucosa (× 6) *B* higher magnification of granuloma (× 55) Note collections of large cells, histiocytes (Hansemann cells)

the fact that in many cases the true nature of the lesion was established only after considerable study and some delay In some patients surgical excision and in others fulguration was performed (Redewill, Cristol and Broders) Lavage with silver nitrate and administration of sulfa drugs orally were tried in a few patients Fulguration was the procedure of choice

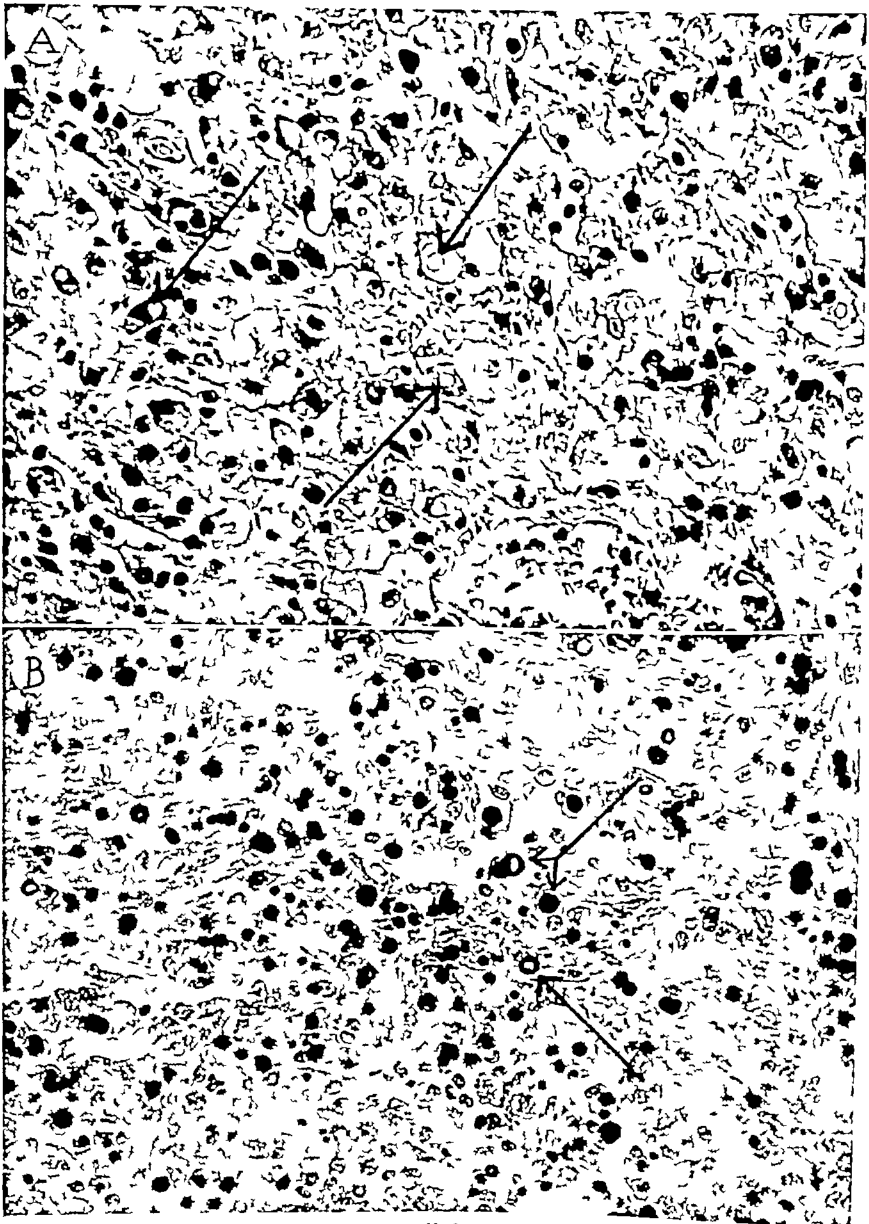

FIG 3 A, trichrome stain Note intracellular inclusions, some laminated (× 525) B, von Kossa stain Note black rings or solid round plaques characteristic appearance of Michaelis Gutmann bodies or calcospheroids (× 525)

REPORT OF CASE

M M, a 64-year-old Italian-American woman, was admitted to the Squier Urological Clinic with hematuria, frequency and burning urination of 3 months' duration Two years prior to the onset of these symptoms, cholecystectomy had been performed. A postoperative hernia and jaundice and pruritus developed. Exploration of the common duct revealed a stricture which required plastic repair. During the course of the operative procedures cystoscopy was performed and the urinary bladder found to be "normal."

The physical examination was essentially negative. The liver edge was palpable at the costal margin. The laboratory findings were as follows: hemoglobin 78 per cent or 11.3 gm., red blood cells 3,770,000 and white blood cells 4,100 per cubic millimeter, the differential was normal. The urine showed four plus albumin, no sugar, and the sediment contained 5–15 red blood cells and 25–30 white blood cells per high power field. The blood urea nitrogen was 50 mg. per cent, the serum chlorides 595 mg. per cent, the serum sodium 132.4 and the potassium 4 mEq per liter. The carbon dioxide combining power was 22 mEq per liter and the serum alkaline phosphatase 20 Bodansky units per 100 cc. There was a faint trace of serum bilirubin. The urine culture grew E. coli.

Radiographic studies of the urinary tract showed renal shadows of normal size, shape and position. The excretory urogram revealed a moderate degree of left hydropelvis and hydroureter. At cystoscopy numerous pinkish-brown, flat nodules were seen distributed throughout the bladder. The picture resembled tumor. The first biopsy was reported as "suspicious of a granular cell myoblastoma." In the second biopsy peculiar cell inclusions were found which in the opinion of several mycologists resembled Cryptococcus neoformans. Special stains (trichrome and von Kossa), however, revealed them to be calcospheroids within histiocytes and led to a diagnosis of malacoplakia. Simple cystectomy with ureterosigmoid transplantation had in the meantime been performed. There was a gradual postoperative drop in blood pressure (from 120/60 to 50/0). Steadily deepening jaundice and a calcium deficiency developed. The patient became comatose, suffered generalized twitchings and convulsions, and died on the fourth postoperative day.

The bladder specimen was an oval soft mass measuring 7 by 5 by 4 cm. On opening it the mucosa revealed numerous soft, raised, pale orange colored nodules (fig. 1). Sections of the latter showed foci of thickened, inflamed submucosa. Within the latter, lymphoid follicles, underlying the urothelium, were present in large numbers, but the outstanding features were numerous large cells or histiocytes (Hansemann cells) and scattered intracellular bodies of calcospheroids, i.e., Michaelis-Gutmann bodies (figs. 2 and 3). The pathologic picture was characteristic of malacoplakia.

SUMMARY AND CONCLUSIONS

An additional case of malacoplakia in a 64-year-old woman has been added to the 67 cases which were culled from a review of available literature.

The disease is more common in females (4 to 1) and its greatest incidence is in the fifth decade.

Malacoplakia is most frequent in the urinary bladder but can involve the ureters and pelves.

The yellowish-brown soft plaques are slightly raised and are composed of histiocytes and lymphocytes Spheroidal bodies of calcium, the calcospheroids or Michaelis-Gutmann bodies, are also characteristic and diagnostic features of this lesion

Differential diagnosis must be made from neoplasm It is to be emphasized that malacoplakia is a granulomatous process of unknown etiology, self-limited course and usually does not require excision of resection Cases have responded well to fulguration

REFERENCES

The bibliography is arranged chronologically and contains a tabulation of the reported cases according to sex, age, and whether diagnosis was made by biopsy, excision or at autopsy

Year	No Cases	Sex	Age	Discovered at
			years	
1902 Michaelis, L and Gutmann, C Ztschr f klin Med **44** 208	2	F	42	Autopsy
		F	46	Autopsy
1903 von Hansemann, D Virchow's Arch f path Anat , **173** 302	2	M	66	Autopsy
		F	77	Autopsy
1903 Fraenkel, E Hamburg Sitzung, Munch med Wschft , **13** 2162 Biol Abt d Aerztl Verein zu Hamburg	1	F	9	Autopsy
1904 Landsteiner, K and Stoerk, O Beitr zur path Anat u z allg Path , Jena, **36** 131	3	F	67	Autopsy
		F	40	Autopsy
		M	Adult	Autopsy
1904 Zenoni, C R Ist Lomb disc a lett Rendic , Milan, Seris 2, **37** 175	1	M	51	Autopsy
1905 Michaelis, L Medizin Klinik, **14** 331 (discussion)	—	—	—	—
1905 Gierke, E Munch med Wschft , **52** 1388	2	F	43	Autopsy
		F	54	Autopsy
1905 Schmorl, K Munch med Wschft , p 1705	1	F	96	Autopsy
1905 Guterbock, R Dissertation Leipzig, B Georgi, 34 pp	1	F	80	Autopsy
		(F,	96,	same as Schmorl's case)
1906 Hagmann, A Monatsberichte f Urol , **6** 86	1	M	28	Operation
1906 Fraenkel, E Verhandl d aerztl Verein zu Hamburg, **5** 23, Deutsche med Wchschft , **32** 818	1	F	78	Autopsy
1906 Hart, K Ztschr f Krebsforschung, **4** 380	1	M	41	Autopsy
1906 Kimla, R Virchow's Arch path Anat , **184** 469, Casop/lek cesk v Praze, **45** 659	3	M	23	Autopsy
		M	37	Autopsy
		M	50	Autopsy
1906 Minelli S Virch Arch f path Anat , **184** 157	1	F	"Old"	Autopsy
1906 Pappenheimer, A M Proc N Y Path Soc N S		F	64	Autopsy
6 65–71	2	F	53	Autopsy
1906 Loth Munch med Wchschft , **59** 1463, Monatsschft f Urol , **11** 90	1	F	72	Autopsy
1906 Vinteler, E N Kharkovskii Meditsinski Zurnal, **1** 45 (not obtainable)	—	—	—	—
1906 von Ellenrieder Dissertation Freiburg i Breisgau (same case as reported by Gierke, 1905)	—	—	—	—
1907 Zangenmeister, W Centralbl f d Krankh d Harn u Sex Org , 496, Ztschr f Urol , **1** 877	1	F	42	Operation

Year	No Cases	Sex	Age	Discovered at
			years	
1907 Wildbolz, H Ztschr f Urol, 1 322	1	M	27	Operation
1909 Berg, G Verhandl der deutschen Gesellschaft f Urologie II Kongress, Berlin, 539	1	F	49	Operation
1909 Betke Aerztlicher Verein zu Frankfurt Sitzung, April 1909	1	F	41	Autopsy
1909 Schmid, H Rev med de la Suisse Romande, 29 757	3	F	41	Autopsy
		F	42	Autopsy
		M	68	Autopsy
1910 Loele, W Beitr zur path Anat u z allg Path Jena, 48 205	1	F	76	Autopsy
1910 Wegelin Cor Bl f schweiz Aerzte, 40 234	1	F	63	Autopsy
1911 Hedrén, G Nord med Ark, 40 1, Nord Med Ark Afd (Kirurgi) Fest f J Berg, Stockholm, #3	1	F	45	Autopsy
1911 Panizzoni Giorn ital d mal ven e d belle, 6 677	1	F	25	Autopsy
1912 Loth Biol Abt d aerztl Verein zu Hamburg, Munch med Wschft, 26 1463	1	F	72	Autopsy
1912 Waldschmidt, M Ztschr f Urologie, 6 541 (same cases as Fraenkel, 1906)	—	—	—	—
1913 Schmidt, H R Frankfurt Ztschr f Path, 14 493	1	F	48	Autopsy
1913 Wetzel, E Virch Arch f path Anat, 214 450	1	M	69	Autopsy
1913 McDonald, S and Sewell, W T J Path & Bact, 18 306	1	F	24	Autopsy
1913 Ferrari, E & Nicholich, G Folio urol, 8 644	1	F	30	Autopsy
1914 Miche, G Contributions à l'étude de la malacoplasie de la vessie (Lausanne) Coutlarv, 1914	1	F	30	Autopsy
1917 v Hoffmann, K R Centrlbl f d Grenzg d Med u Chir, 19 34 (a discussion)	—	—	—	—
1917 English, J Ztschr f Urol, 1 641	1	M	28	Autopsy
1918 Blum, V Ztschr f Urol, 12 401	1	F	40	Cyst
1919 Folsom, AL J A M A, 73 1112	2	F	43	Cyst
		F	?	Cyst
1921 Ramcke, R E Ztschr f Urol, 15 92	2	F	51	Autopsy
		F	63	Autopsy
1922 Oestreich, R Beitr z path Anat u z allg Path, 70 342	1	M	51	Autopsy
1922 Thomson Walker, J Barrington, F Proc Roy Soc Med, 16 32	1	F	43	Autopsy
1924 Demel, V C Pathologica, 16 531 & 559	1	F	29	Autopsy
1926 Heilmann, P Beitr z path Anat u z allg Path, 75 216	1	F	73	Autopsy
1924 Opperman, E Ztschr f Urol, 18 365	1	F	8	Autopsy
1927 Dickson, W E C, Gray, A C E and Kidd, F Urol & Cut Rev, 31 611	1	F	24	Biopsy
1927 Kairis, Z Virch Arch f path Anat, 266 788	1	F	15 mos	Cyst
1929 Redewill, F H J A M A, 92 532	1	M	62	Biopsy
1934 Chisholm, A L and Tudhope, G R Edin Med J, 41 626	1	F	61	Operation
1938 Wells H G Arch Path, 26 32 (discussion)	—	—	—	—
1939 Rudnick D F and Ragins, A B *J Urol*, 42 *108*, Rev in Yr Bk Urol, 1939, p 183	1	F	53	Operation

Year	No Cases	Sex	Age	Discovered at
			years	
1943 Redewill, F H J Urol , **49** 401	1	F	40	Biposy
1944 Morison, J E J Path & Bact , **56** 67	1	F	6	Autopsy
1946 Cristol, D S and Broders A C J Urol , **55** 260	2	F	42	Biopsy
		F	35	Biopsy
1950 Boonstra, C E and Bates P L U S Armed Forces M J , **1** 1029, Rev in Yr Bk Urol , 1950, p 224	1	F	25	Autopsy
1951 Bunting, H A M A Arch Path , **52** 458 (discussion)	—	—	—	—
1951 Hagemann, E Ztschr f Urol , **44** 9	1	F	31	Biopsy
1951 French, A J and Mason J T J Urol , **66** 229	1	F	41	Biopsy
1952 Bleisch, V R and Konikov, N F A M A Arch Path , **54** 388, Rev in Yr Bk Urol , 1953-4, p 224	4	F	41	Autopsy
		F	44	Autopsy
		F	74	Autopsy
		F	46	Autopsy
1956 Melicow, M M J Urol , this issue	1	F	64	Biopsy

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TOTAL CYSTECTOMY ANALYSIS OF 225 CASES FROM THE BLADDER TUMOR REGISTRY

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This investigation was undertaken in an attempt to evaluate the results of treatment of carcinoma of the bladder by simple cystectomy For this purpose a followup period of at least 5 years is essential, therefore, the cases selected were those that had been contributed to the Bladder Tumor Registry of the American Urological Association at the Armed Forces Institute of Pathology prior to May 1, 1951, the earliest cystectomy reported to the Registry having been performed in June 1931 Of the total of 312 cases registered only 225 included sufficient data to make them acceptable for our study

Of the 225 cases, 110 were submitted by government hospitals and the remaining 115 by civilian contributors Original clinical records were borrowed from civilian hospitals and Armed Forces repositories, and followup questionnaires were sent to physicians or to patients Histologic sections were again reviewed and the tumors reclassified pathologically Autopsy protocols, when available, were studied

Only 4 patients in the group were untraced after cystectomy, thus, information subsequent to operation was available for 221, or 98 per cent, of the patients Three of the 221 were lost to followup less than 5 years after cystectomy, 37 survived 5 years or longer and 21 of these were living at last report

Our study will consider pathologic classification, clinical data, methods of ureteral disposition, survival rates and causes of death

PATHOLOGICAL CLASSIFICATION

The 225 tumors in this study were classified according to the Bladder Tumor Registry's new criteria, which are based entirely on the histologic appearance of the tumor Thus, papillary tumors in which the epithelium is indistinguishable from the bladder epithelium are classified as papilloma, those showing anaplasia, increased mitotic activity, thickening or lack of differentiation of the epithelium, as papillary carcinoma, grade 1 Those with a moderate degree of anaplasia and lack of differentiation are classified as grade 2 carcinoma (papillary, papillary and infiltrating, or initially infiltrating), while those with marked anaplasia or complete loss of differentiation are placed in the category, grade 3 carcinoma (papillary, papillary and infiltrating, or initially infiltrating) Pure squamous carcinomas and adenocarcinomas of the bladder are similarly classified

There were no patients with papilloma or papillary carcinoma, grade 1

Thirty-one of the 225 patients (14 per cent) had papillary carcinoma, grade 2,

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Read at annual meeting of American Urological Association, Boston, Mass May 29-June 1 1956

70 (31 per cent), papillary and infiltrating carcinoma, grade 2, 65 (29 per cent), papillary and infiltrating carcinoma, grade 3, 30 (13 per cent), infiltrating carcinoma, grades 2 and 3, and 29 (13 per cent), infiltrating squamous carcinoma, grades 2 and 3

The depth of infiltration of the neoplasms could not be determined because the gross specimens were not available to us, but vascular invasion by tumor cells could be demonstrated in the histologic sections Such invasion was seen in 62 cases 17 of papillary and infiltrating carcinoma, grade 2, 23 of papillary and infiltrating carcinoma, grade 3, 12 of infiltrating carcinoma, grades 2 and 3, and 10 of squamous infiltrating carcinoma, grades 2 and 3

CLINICAL DATA

Age at cystectomy (table 1) Eighty per cent of all patients were 50 years of age or over The youngest patient was a man 22 years of age, with papillary and infiltrating carcinoma, grade 2

This patient had hematuria which began when he was 19 years old Segmental resection of a papillary carcinoma situated along the mural ureter was followed by numerous recurrences over a period of 3 years These were treated by transurethral fulguration and radium bomb Because of the progress of the malignant tumor, the radiation effects in the bladder, and hydroureter and hydronephrosis of the left kidney, cystectomy with ureteroenterostomy (Wattenberg-Beare technique) was performed when the patient was 22 years of age Drainage from the left kidney proved to be inadequate, and nephrostomy and reimplantation were performed 5 months later Continued adequate drainage permitted closure of the nephrostomy and the patient was discharged Three months later when he was hospitalized for checkup, acute intestinal obstruction developed as the result of herniation of a loop of jejunum underneath the right ureteroenterostomy Resection of the gangrenous loop of jejunum and extraperitonization of the right ureteroenterostomy were successful, but the patient died 7 days later of massive pulmonary embolism Postmortem examination revealed moderate hydronephro-

TABLE 1 *Age distribution in diagnostic groups at time of total cystectomy*

Age Group	Diagnostic Group					
	Total	Pap 2	Pap Inf 2	Pap Inf 3	Inf 2 3	Sq Inf 2-3
Total with age stated	221	30	70	64	29	28
20–29 years	3		3			
30–39 years	10	2	3	1	1	3
40–49 years	30	5	7	7	5	6
50–59 years	98	9	34	30	13	12
60–69 years	69	12	20	22	9	6
70–79 years	11	2	3	4	1	1
Average age*	56	57	55	57	55	54

*Averages based on actual ages rather than on grouped data

TABLE 2 *Diagnostic group in relation to sex Total cystectomy*

Diagnostic Group	Number			Per Cent	
	Total	Male	Female	Male	Female
Total	225	200	25	89	11
Papillary 2	31	27	4	87	13
Papillary-infiltrating 2	70	63	7	90	10
Papillary infiltrating 3	65	57	8	88	12
Infiltrating 2 and 3	30	28	2	93	7
Squamous infiltrating 2 and 3	29	25	4	86	14

sis and hydroureter on the left side and severe acute and chronic bilateral pyelonephritis

The two oldest patients were 74-year-old men one with papillary carcinoma grade 2 the other with infiltrating carcinoma, grade 3 In the entire group there was no evidence of association between age at time of cystectomy and pathologic diagnosis The average age of patients both male and female in all diagnostic groups was 56 years

Sex (table 2) The sex preponderance in this series was on the side of the male in the ratio of 8 to 1 Of the 5778 cases with sex recorded in the Bladder Tumor

TABLE 3 *Incidence of specific symptoms in relation to age at onset Total cystectomy*

Age at Onset	Number of Patients*	Symptom			
		Hematuria	Dysuria	Frequency	Urgency
		Number			
Total	210	186	100	112	25
20-29	8†	4	5	4	2
30-39	10	8	5	7	2
40-49	35	33	18	17	2
50-59	104	96	49	57	11
60-69	45	37	20	25	8
70-79	8	8	3	2	
		Per Cent in Age Group			
Total	210	89	48	53	12
20-29	8†	50	63	50	25
30-39	10	80	50	70	20
40-49	35	94	51	49	6
50-59	104	92	47	55	11
60-69	45	82	44	56	18
70-79	8	100	38	25	

* Number of patients with recorded symptoms

† Includes 1 patient age 19

Note The average age at onset was 54 years median age 55 and the range was 19 through 73 years

Registry by 1951, 4535 (78 per cent) were males and 1243 (22 per cent) were females In comparison with these figures, the 200 male patients with total cystectomy comprised 4 4 per cent of all the males in the Registry, while the 25 females represented only 2 0 per cent of all the females It would appear that there is either a reluctance on the part of the female patient to accept this operation, or on the part of the physician to advise it

Symptoms (table 3) The four major symptoms of bladder tumor—hematuria, dysuria, frequency and urgency—were investigated in relation to the ages of the patients at onset Total gross hematuria was the sole symptom in 59 cases Statistical evidence of an association between age at onset and hematuria, with or without other urinary symptoms, is seen in this study

Initial treatment (tables 4, 5, 6 and 7) Cystectomy was the initial therapy in 125 cases (56 per cent) More conservative measures of various kinds were employed in 100 cases (44 per cent) before cystectomy (table 4) Transurethral resection or fulguration without irradiation, or both, was the initial treatment in the majority of this group (55 of 100 patients) Open surgical procedures, namely, segmental or transvesical transections without irradiation, were performed on 27

TABLE 4 *Initial treatment of patients with total cystectomy*

Type of Treatment	Number	Per Cent
Total	225	100
Cystectomy	125	56
Other than cystectomy*		
Radiation alone	8	4
Open surgery without radiation	27	12
Open surgery with radiation	7	3
Closed surgery without radiation	55	24
Closed surgery with radiation	3	1

* Radiation—Radon implantation and/or x ray
Open surgery—Cystotomy
Closed surgery—Operation performed by transurethral approach

TABLE 5 *Duration from initial treatment to cystectomy (treatment prior to cystectomy)*

Duration	Number
Total	100
Less than 6 months	21
6 months	16
1 year	17
2 years	13
3 years	4
4 years	10
5 years and over	19

Note The longest interval was 20 years

TABLE 6 *Duration from diagnosis to total cystectomy (no treatment prior to cystectomy)*

Duration	Number	Per Cent
Total with cystectomy as initial treatment	125	100
Less than 1 month	43	35
1 month	36	29
2 months	20	16
3 months	9	7
4 months	7	6
5 months	3	2
6 months	3	2
Over 6 months	4	3

Note The average duration was 1.8 months. The longest interval was 12 months.

other patients. Radiation with or without surgical measures was utilized for the 18 remaining patients of this group. The cases in our series antedated the introduction of radioactive isotopes and all irradiation therapy was by implantation of radon seeds or by external irradiation.

The time lapse between the initial treatment and cystectomy in these 100 patients was determined (table 5). Cystectomy was performed on 37 patients within the year following initial treatment. In 29, cystectomy was delayed from 4 to 20 years after treatment of other types.

Of the 125 patients for whom cystectomy was the initial treatment (table 6), 80 per cent had the operation within 2 months, 64 per cent within 1 month, of the diagnosis. The average interval between diagnosis and cystectomy was 1.8 months. In only one instance was the operation delayed as long as 12 *months after* the diagnosis, with no treatment in the interim.

TABLE 7 *Initial treatment by diagnostic group. Total cystectomy*

Diagnostic Group	Initial Treatment: Total	Initial Treatment: Cystectomy	Initial Treatment: Other than cystectomy
	Number		
Total	225	125	100
Papillary 2	31	12	19
Papillary infiltrating 2	70	35	35
Papillary infiltrating 3	65	42	23
Infiltrating 2 and 3	30	17	13
Squamous infiltrating 2 and 3	29	19	10
	Per Cent		
Papillary 2	100	39	61
Papillary infiltrating 2	100	50	50
Papillary infiltrating 3	100	65	35
Infiltrating 2 and 3	100	57	43
Squamous infiltrating 2 and 3	100	66	34

Registry by 1951, 4535 (78 per cent) were males and 1243 (22 per cent) were females In comparison with these figures, the 200 male patients with total cystectomy comprised 4 4 per cent of all the males in the Registry, while the 25 females represented only 2 0 per cent of all the females It would appear that there is either a reluctance on the part of the female patient to accept this operation, or on the part of the physician to advise it

Symptoms (table 3) The four major symptoms of bladder tumor—hematuria, dysuria, frequency and urgency—were investigated in relation to the ages of the patients at onset Total gross hematuria was the sole symptom in 59 cases Statistical evidence of an association between age at onset and hematuria, with or without other urinary symptoms, is seen in this study

Initial treatment (tables 4, 5, 6 and 7) Cystectomy was the initial therapy in 125 cases (56 per cent) More conservative measures of various kinds were employed in 100 cases (44 per cent) before cystectomy (table 4) Transurethral resection or fulguration without irradiation, or both, was the initial treatment in the majority of this group (55 of 100 patients) Open surgical procedures, namely, segmental or transvesical transections without irradiation, were performed on 27

TABLE 4 *Initial treatment of patients with total cystectomy*

Type of Treatment	Number	Per Cent
Total	225	100
Cystectomy	125	56
Other than cystectomy*		
Radiation alone	8	4
Open surgery without radiation	27	12
Open surgery with radiation	7	3
Closed surgery without radiation	55	24
Closed surgery with radiation	3	1

* Radiation—Radon implantation and/or x ray
Open surgery—Cystotomy
Closed surgery—Operation performed by transurethral approach

TABLE 5 *Duration from initial treatment to cystectomy (treatment prior to cystectomy)*

Duration	Number
Total	100
Less than 6 months	21
6 months	16
1 year	17
2 years	13
3 years	4
4 years	10
5 years and over	19

Note The longest interval was 20 years

Table 6 *Duration from diagnosis to total cystectomy (no treatment prior to cystectomy)*

Duration	Number	Per Cent
Total with cystectomy as initial treatment	125	100
Less than 1 month	43	35
1 month	36	29
2 months	20	16
3 months	9	7
4 months	7	6
5 months	3	2
6 months	3	2
Over 6 months	4	3

Note The average duration was 1 8 months The longest interval was 12 months

other patients Radiation with or without surgical measures was utilized for the 18 remaining patients of this group The cases in our series antedated the introduction of radioactive isotopes and all irradiation therapy was by implantation of radon seeds or by external irradiation

The time lapse between the initial treatment and cystectomy in these 100 patients was determined (table 5) Cystectomy was performed on 37 patients within the year following initial treatment In 29, cystectomy was delayed from 4 to 20 years after treatment of other types

Of the 125 patients for whom cystectomy was the initial treatment (table 6), 80 per cent had the operation within 2 months, 64 per cent within 1 month, of the diagnosis The average interval between diagnosis and cystectomy was 1 8 months In only one instance was the operation delayed as long as 12 months after the diagnosis, with no treatment in the interim

Table 7 *Initial treatment by diagnostic group Total cystectomy*

Diagnostic Group	Initial Treatment		
	Total	Cystectomy	Other than cystectomy
	Number		
Total	225	125	100
Papillary 2	31	12	19
Papillary infiltrating 2	70	35	35
Papillary infiltrating 3	65	42	23
Infiltrating 2 and 3	30	17	13
Squamous infiltrating 2 and 3	29	19	10
	Per Cent		
Papillary 2	100	39	61
Papillary infiltrating 2	100	50	50
Papillary infiltrating 3	100	65	35
Infiltrating 2 and 3	100	57	43
Squamous infiltrating 2 and 3	100	66	34

Registry by 1951, 4535 (78 per cent) were males and 1243 (22 per cent) were females. In comparison with these figures, the 200 male patients with total cystectomy comprised 4.4 per cent of all the males in the Registry, while the 25 females represented only 2.0 per cent of all the females. It would appear that there is either a reluctance on the part of the female patient to accept this operation, or on the part of the physician to advise it.

Symptoms (table 3). The four major symptoms of bladder tumor—hematuria, dysuria, frequency and urgency—were investigated in relation to the ages of the patients at onset. Total gross hematuria was the sole symptom in 59 cases. Statistical evidence of an association between age at onset and hematuria, with or without other urinary symptoms, is seen in this study.

Initial treatment (tables 4, 5, 6 and 7). Cystectomy was the initial therapy in 125 cases (56 per cent). More conservative measures of various kinds were employed in 100 cases (44 per cent) before cystectomy (table 4). Transurethral resection or fulguration without irradiation, or both, was the initial treatment in the majority of this group (55 of 100 patients). Open surgical procedures, namely, segmental or transvesical transections without irradiation, were performed on 27

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* Radiation—Radon implantation and/or x-ray.
Open surgery—Cystotomy.
Closed surgery—Operation performed by transurethral approach.

TABLE 5. *Duration from initial treatment to cystectomy (treatment prior to cystectomy)*

Duration	Number
Total	100
Less than 6 months	21
6 months	16
1 year	17
2 years	13
3 years	4
4 years	10
5 years and over	19

Note. The longest interval was 20 years.

TABLE 9 *Five year survival in each diagnostic group following total cystectomy*

Diagnostic Group	Total with Data	Survived Years or Over	
		Number	Per cent
Total with data	218*	37	17
Papillary 2	30	8	27
Papillary-infiltrating 2	68	16	24
Papillary-infiltrating 3	62	9	15
Infiltrating 2 and 3	29	3	10
Squamous infiltrating 2 and 3	29	1	3

* Excludes 4 patients on whom no information was available after cystectomy, and 3 patients who were lost before the end of 5 years

TABLE 10 *Survival rates following total cystectomy in relation to initial treatment*

Months after Cystectomy	Initial Treatment	
	Cystectomy	Other than cystectomy
0	100	100
6	67	67
12	47	50
18	37	38
24	28	29
30	27	22
36	26	22
42	26	20
48	24	18
54	21	16
60	20	15
Number of patients*	123	98

* Excludes 4 patients who were lost to followup after cystectomy

SURVIVAL RATES

The overall 5-year survival rate in this series was 17 per cent (tables 9 10, 11 and fig 1) Of the entire group of 218 patients (225 minus 4 patients untraced after operation and 3 patients lost to followup less than 5 years after total cystectomy), 181 were known to be dead in 5 years and 37 living for 5 years or more Sixteen of the patients who survived 5 years are known to have died within 6½ years after cystectomy

The survival rates, however, varied considerably for the different diagnostic groups the rate was 27 per cent for papillary carcinoma, grade 2, 24 per cent for papillary and infiltrating carcinoma, grade 2, 15 per cent for papillary and infiltrating carcinoma, grade 3, 10 per cent for infiltrating carcinoma, grades 2 and 3, and 3 per cent for squamous and infiltrating carcinoma, grades 2 and 3

The graph shows the survival rates calculated by the actuarial method * In

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* Berkson J and Gage, R P Proc Staff Meet, Mayo Clinic, 25 270–286, 1950

As might be expected, there is statistical evidence of an association between the initial treatment and the pathological diagnosis (table 7). Nineteen, or 61 per cent, of the 31 patients with noninfiltrating tumors received treatment other than cystectomy initially as compared with 81, or 42 per cent, of the 194 patients with infiltrating tumors.

Ureteral disposition (table 8). Bilateral ureterointestinal anastomosis in association with cystectomy, either as a one-stage or two-stage operation, was performed in 186 instances (84 per cent), but subsequently secondary bilateral cutaneous ureterostomy was done in eight of these. In five additional patients diversion of one of the transplanted ureters to the skin was accomplished at a later date.

The grade of the tumor did not influence the choice of operation, 86 per cent of the patients with noninfiltrating, and 81 per cent of those with infiltrating tumors were treated by cystectomy and transplantation of the ureters to the intestine. On the other hand, the method employed was governed to some extent by the operation in favor at the time. For example, 26 per cent of the 38 cutaneous ureterostomies as against 3 per cent of the 186 ureterointestinal anastomoses were performed in the years prior to 1940.

The surgical technique employed in ureterointestinal anastomosis was known for only 76 patients, but in 82 per cent of these the Coffey methods 1 and 2 were used.

TABLE 8. *Diagnostic groups in relation to ureteral disposition. Total cystectomy*

Diagnostic Group	Total	Disposition of Ureters		
		Intestinal	Cutaneous	Intestino-cutaneous
	Number			
Total with data	221	173	38*	10†
Papillary 2	29	25	4	
Papillary infiltrating 2	69	51	15	3
Papillary-infiltrating 3	64	52	8	4
Infiltrating 2 and 3	30	24	5	1
Squamous infiltrating 2 and 3	29	21	6	2
	Per Cent			
Total with data	100	78	17 *	5 †
Papillary 2	100	86	14	
Papillary infiltrating 2	100	74	22	4
Papillary infiltrating 3	100	81	13	6
Infiltrating 2 and 3	100	80	17	3
Squamous infiltrating 2 and 3	100	72	21	7

* Includes 8 patients who had ureterointestinal anastomosis with later secondary cutaneous ureterostomy.

† Includes 4 patients who had transplantation of both ureters to intestine with later change of one ureter to skin, and 1 patient with one ureter to intestine and one nephrostomy.

TABLE 9 *Five-year survival in each diagnostic group following total cystectomy*

Diagnostic Group	Total with Data	Survived 5 Years or Over	
		Number	Per cent
Total with data	218*	37	17
Papillary 2	30	8	27
Papillary-infiltrating 2	68	16	24
Papillary-infiltrating 3	62	9	15
Infiltrating 2 and 3	29	3	10
Squamous infiltrating 2 and 3	29	1	3

* Excludes 4 patients on whom no information was available after cystectomy, and 3 patients who were lost before the end of 5 years

TABLE 10 *Survival rates following total cystectomy in relation to initial treatment*

Months after Cystectomy	Initial Treatment	
	Cystectomy	Other than cystectomy
0	100	100
6	67	67
12	47	50
18	37	38
24	28	29
30	27	22
36	26	22
42	26	20
48	24	18
54	21	16
60	20	15
Number of patients*	123	98

* Excludes 4 patients who were lost to followup after cystectomy

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The overall 5-year survival rate in this series was 17 per cent (tables 9, 10, 11 and fig 1) Of the entire group of 218 patients (225 minus 4 patients untraced after operation and 3 patients lost to followup less than 5 years after total cystectomy), 181 were known to be dead in 5 years and 37 living for 5 years or more Sixteen of the patients who survived 5 years are known to have died within 6½ years after cystectomy

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The graph shows the survival rates calculated by the actuarial method * In

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* Berkson J and Gage, R P Proc Staff Meet , Mayo Clinic, 25 270–286, 1950

TABLE 11 *Survival rates from total cystectomy in relation to ureteral disposition*

Months following Cystectomy	Disposition of Ureters	
	Intestinal	Cutaneous*
0	100	100
6	71	55
12	52	34
18	39	34
24	29	26
30	26	21
36	25	21
42	24	18
48	23	16
54	19	16
60	19	13
Number of patients	170	38

* Includes 8 patients who had ureterointestinal anastomosis with later change of ureters to skin

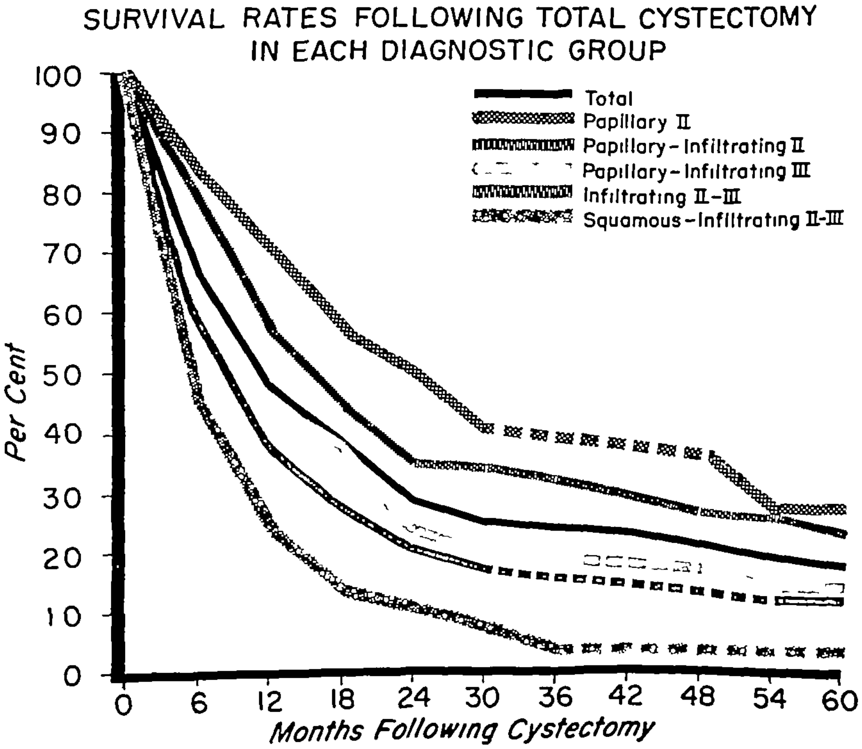

FIG 1

contrast to the direct method employed in table 9, in which only those followed for 5 years or longer are taken into account, by the actuarial method the data are based on 221 patients including the 3 patients who were lost to followup in less than 5 years The broken lines in the graph signify that no deaths occurred in those periods

The data indicate that although only 67 per cent of the 221 patients with total cystectomy survived more than 6 months, the survival rates varied from 83 per cent for patients with papillary carcinoma, grade 2, to 45 per cent for patients with squamous carcinoma, infiltrating grades 2 and 3 Less than half the entire group survived more than 1 year after cystectomy, however, 70 per cent of those with papillary carcinoma, grade 2, were alive, whereas 24 per cent of those with squamous carcinoma, grades 2 and 3 (infiltrating), were alive The slight discrepancy between the data utilized in the graph and those recorded on table 9 is explained by the fact that the figures in the former are based on 221 patients and in the latter on 218 patients

Patients with cystectomy as the initial treatment had a 5-year survival rate of 20 per cent in contrast to 15 per cent for those who had treatment of other types prior to cystectomy (table 10) Sixty-one per cent of the patients with noninfiltrating tumor had initial treatment other than cystectomy as against 42 per cent with infiltrating tumor

Of interest is the disclosure that 5-year survival rates in this series appear to be better for patients who had ureteroenterostomies than for those who had cutaneous ureterostomies—19 per cent against 13 per cent (table 11)

Cause and time of death (table 12) Information relative to the time and cause of death is based on autopsy protocols available in the Registry (60 cases) or data supplied by the attending physician in the remaining cases Of the 197 patients who were known to be dead, 25 survived less than 1 month Sixteen of these 25

TABLE 12 *Reported cause of death and interval from total cystectomy to death*

Reported Cause of Death	Interval after Total Cystectomy (months)									
	Total	Less than 1 month	1–	6–11	12–17	18–23	24–	36–47	48–59	60 and over
Total known dead	197	25	48	41	24	20	9	6	8	16
Kidney infection	77	7	20	21	9	6	3	4	2	5
With carcinomatosis	*39*		*9*	*15*	*4*	*4*	*2*	*1*	*1*	*3*
Without carcinomatosis	*38*	*7*	*11*	*6*	*5*	*2*	*1*	*3*	*1*	*2*
Carcinomatosis	65	7	12	12	10	9	4	1	3	7
Peritonitis	7	3	2	1					1	
Septicemia	2	1	1							
Pneumonia or pulmonary infection	7	2	2	1	1	1				
Cardiovascular accident*	14	2	2		2		2	1	1	4
Unknown	25	3	9	6	2	4			1	

* Includes one patient who died of massive hemorrhage the site undetermined

patients died within 10 days, 6 of them within 2 days of the operation, and 9 between the eleventh and twenty-fifth day. Of the remaining 172 patients, 156 died within the first 5 years and 16 died 5 years or more after cystectomy.

The cause of death was unknown in 25 of the 197 patients known to have died. Seventy-seven, almost equally divided between those with and those without carcinomatosis, died of kidney infection. In the group of 39 patients with carcinomatosis, all of whom survived more than 1 month, 36 died within 5 years (1 from carcinoma of the liver with no recurrence or metastasis of the bladder tumor), and 3 after 5 years. Of 38 patients without carcinomatosis, 3 died within 10 days of cystectomy, 4 others died within 30 days, 29 survived more than 1 month but died within 5 years, and 2 died after 5 years.

Sixty-five patients died of carcinomatosis: 7 in less than 1 month, 51 within 5 years, and 7 others more than 5 years after cystectomy. Included in the last group, however, were one patient with carcinoma of prostate with metastasis and one with carcinoma of colon with metastasis; neither patient had shown evidence of carcinoma of bladder either locally or distally during the more than 5 years following total cystectomy.

Seven patients died of peritonitis and intestinal obstruction, 2 within 10 days and another within 30 days of cystectomy, 2 of septicemia, 1 of them within 30

TABLE 13 *Reported cause of death in relation to ureteral disposition Total cystectomy*

Cause of Death	Total with Data	Ureteral Disposition		
		Intestinal	Cutaneous	Intestino-cutaneous*
	Number			
Total	169†	133	26	10
Kidney infection	75	58	14	3
Carcinomatosis	64	53	6	5
Peritonitis, intestinal obstruction	7	6	1	
Septicemia	2	1	1	
Pneumonia, pulmonary infection	7	5	1	1
Cardiovascular disease	14	10	3	1
	Per Cent by Disposition			
Total	100	100	100	100
Kidney infection	45	44	54	30
Carcinomatosis	38	40	23	50
Peritonitis, intestinal obstruction	4	4	4	
Septicemia	1	1	4	
Pneumonia, pulmonary infection	4	4	4	10
Cardiovascular disease	8	7	11	10

* One ureter to the intestine and the other ureter a cutaneous transplant

† Excludes 28 patients with insufficient data as follows: in 24 cause of death not reported, in 1 disposition of ureter and cause of death not reported, in 3 disposition of ureters not reported

days 7 of pneumonia or pulmonary infection, including 1 who died within 10 days and 1 within 30 days, 14 of cardiovascular accident 2 within 1 month 8 others within 5 years and 4 after 5 years

Cause of death and disposition of ureters (table 13) Of 169 patients in whom the cause of death and the disposition of the ureters were known 133 had ureterointestinal anastomosis, 26 ureterocutaneous, and 10 both (one ureter to skin, one to intestine) Forty-four per cent of those with ureteroenterostomies died of renal infection in contrast to 54 per cent of those with ureterocutaneous anastomosis, and 30 per cent of those with one ureterointestinal and one ureterocutaneous anastomosis Forty per cent of those with ureteroenterostomies died of carcinomatosis in comparison with 23 per cent of those with ureterocutaneous and 50 per cent of those with both

DISCUSSION

The 5-year survival rate of 17 per cent for the 225 patients from the Bladder Tumor Registry treated by total cystectomy, while discouragingly low, is comparable with those reported by Jewett and Strong Ferris and Priestley Colby and Kerr, Flocks, Marshall and Whitmore, and Drinker and O'Conor

The survival rates are better than those for untreated patients Welch and Nathanson reported survival rates of 50 per cent and 10 per cent for 14 months and 60 months, respectively, for such patients and Prout and Marshall, in reviewing the literature on the subject and including their own 59 cases, reported survival rates of 38 per cent and 4 per cent for 1 and 5 years, respectively

The survival rates of the patients with carcinoma of the bladder treated by total cystectomy are lower than those of patients with bladder tumor (irrespective of therapy) reported from the Registry Dean and associates reported a 5-year survival rate of 39 per cent for the first 1400 cases in the Bladder Tumor Registry (all cases received prior to 1935) *

Only a few of the patients in that series were treated by total cystectomy From a study of 135 consecutive cases of cancer of the bladder treated by various methods, Royce and Ackerman reported a 5-year survival rate of 28 per cent For the 77 patients with definitely malignant tumors (excluding those with tumors graded 1) the average length of survival was 1 year and 7 months, and only 9 per cent survived 5 years

Recently Brice Marshall, Green and Whitmore have reported on survival of 156 patients after simple cystectomy The survival rates ranged from 75 per cent and 47.2 per cent for 1 and 5 years respectively, in tumors of low grades of malignancy (grades 1 and 2 and stages O A, or B) to 39.2 per cent and 8 8 per cent for 1 and 5 years, respectively, in tumors of higher grades of malignancy (grades 3 and 4, and stages B, C or D) For their stage D patients, the 1-year survival was 33 3 per cent and the 5-year, 4.2 per cent These rates, although distinctly better than those we are reporting, as well as those of others referred to in this dis-patients died within 10 days, 6 of them within 2 days of the operation, and 9 between the eleventh and twenty-fifth day Of the remaining 172 patients, 156 died within the first 5 years and 16 died 5 years or more after cystectomy

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* The 5-year survival rate of 49 per cent for carcinoma of the bladder irrespective of grading reported in another recent study from the Registry is not comparable, because the patients were limited to those with initial carcinoma of the bladder without demonstrable metastases

The cause of death was unknown in 25 of the 197 patients known to have died Seventy-seven, almost equally divided between those with and those without carcinomatosis, died of kidney infection In the group of 39 patients with carcinomatosis, all of whom survived more than 1 month, 36 died within 5 years (1 from carcinoma of the liver with no recurrence or metastasis of the bladder tumor), and 3 after 5 years Of 38 patients without carcinomatosis, 3 died within 10 days of cystectomy, 4 others died within 30 days, 29 survived more than 1 month but died within 5 years, and 2 died after 5 years

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cussion, compare unfavorably with the survival rates for patients with bladder carcinoma treated by simple segmental resection Marshall and associates reported survival rates of 60 4 per cent and 29 1 per cent for 1 and 5 years respectively after segmental resection in 48 patients with "high grade and *high stage*" carcinoma of bladder, and Mostofi reported survival rates of 43 per cent and 34 per cent, respectively, for patients who had initial carcinoma of bladder, grades 2 and 3, infiltrating types, and who were treated by segmental resection alone

An analysis of the surprisingly high mortality rates must take into consideration the type of patients selected for cystectomy, the specific justification for the operation, the period in which the operation was performed, the experience and dexterity of the urologist and the adequacy of the preoperative preparation, operative technique and postoperative care Unfortunately, the information available to us did not include such details

Analysis of the causes of death in our series shows that of the 172 patients for whom we had information, 68 had no evidence of carcinoma of bladder at the time of death, 14 died of cardiovascular accident, 16 of extrarenal infection and 38 of kidney infection One hundred four patients died of carcinomatosis but in 3 of these the primary tumor was not of bladder in 1 it was of prostate, in 1, of liver, and in the third, of colon Thirty-eight of the remaining 101 patients had renal infections and 63 did not

A certain proportion of the deaths among patients with total cystectomy may be considered preventable, either by early and complete removal of the tumor or by control of infection Cordonnier and Lage have pleaded for more accurate evaluation of tumors with earlier decision for cystectomy Leadbetter and Cooper and Whitmore and Marshall have advocated more radical procedures to include dissection of lymph nodes and pelvic exenteration However, Marshall and Whitmore consider the presence of more than one or two positive lymph nodes or evidence of distant metastasis a contraindication to radical surgical procedures

Improvement in survival rates is certain in this age of antibiotics and isotopes Surgical mortality rates have already been reduced materially with advances in anesthesia, availability of whole blood, better understanding of blood electrolytes and more thorough preparation of patients Cordonnier and Lage reported 54 consecutive operations without an operative death

The use of isolated bowel segments as urinary receptacles may reduce infection of the urinary tract, and earlier cystectomy should have the effect of preventing recurrence and metastases in some instances Whether such measures will materially improve the survival rates of patients after total cystectomy is yet to be determined

SUMMARY

Two hundred twenty-five patients from the Bladder Tumor Registry on whom total cystectomy was performed either as initial or subsequent treatment for carcinoma of the bladder had an overall 5 year survival rate of 17 per cent The rates were more favorable for papillary (noninfiltrating) carcinoma, grade 2 (27 per cent) and for papillary and infiltrating carcinoma, grade 2 (24 per cent) than for tumors of higher grades of malignancy Discouraging as these results may be, it must be realized that the cases reported here are a selected group and a substantial number were treated before the advent of antibiotics Early diagnosis and complete removal of the tumor and control of infection will undoubtedly improve the survival rates

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TRAUMATIC RUPTURE OF THE TESTICLE

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Rupture of the testicle without direct penetration of the scrotal skin has rarely been reported A review of the literature reveals only 19 cases recorded to this date, and our experience with 2 cases of rupture of the testicle would lead us to believe that many of the cases of hematocele following trauma are probably associated with an underlying rupture of the testicle If these cases are explored shortly after injury, rather than treated by conservative measures such as aspiration and scrotal support, it is probable that in many cases the testicle may be surgically repaired, and atrophy or delayed orchiectomy prevented

The cases to be reported illustrate in one instance a rupture through the tunica albuginea with eventration of the testicular tissue into the tunica vaginalis In the other, injury resulted in rupture and partial necrosis of the testicular tissue within the tunica albuginea In both cases early surgical exploration following trauma resulted in a preservation of the major portion of the testicle involved

CASE REPORTS

Case 1 A 15-year-old white man was admitted to the Jewish General Hospital, December 22, 1952, with a history of having been struck in the scrotum while playing hockey, 3 hours prior to admission to hospital Following the injury he experienced severe pain and swelling of the left side of the scrotum, with associated nausea and weakness He was seen by his family physician who administered 75 mg demerol, and referred the patient for examination and treatment, because of an expanding mass in the left side of the scrotum On admission to hospital the patient complained of moderate pain in the left side of the scrotum with slight nausea He exhibited a moderate pallor The blood pressure was 130 over 75 millimeters of mercury The pulse was 78 per minute Temperature was 98 4 degrees Physical examination other than the local lesion was not remarkable Examination of the scrotal contents revealed a large swelling and redness of the left side of the scrotum The left testicle appeared to be enlarged to approximately three times normal size The epididymis could not be localized There was considerable pain on palpation of the left spermatic cord and testicle Urinalysis was negative Hemoglobin was 12 9 gm per cent White blood count was 8100 per cubic millimeter A diagnosis of traumatic hematocele with possible torsion of the testis on the left side was made, and surgical exploration of the scrotum was performed 4 hours following the initial injury

Under spinal anesthesia a left scrotal incision was made and the tunica vaginalis exposed There was considerable bloody fluid within the tunica vaginalis On opening the latter, bloody fluid escaped under pressure and the left testis presented the following picture A large blood clot covered the anterior surface of the testis and upon removing it there was noted a complete transverse rupture

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of the tunica albuginea with eventration of the testicular tissue Upon removing the blood clot a small bleeding artery was seen at the angle of the ruptured tunica This was clamped and ligated and an attempt made to replace the bulging testicular tissue which showed no apparent impairment of blood supply It was found that the tunica albuginea could not completely cover the herniated testicular contents and so a partial repair of the tunica albuginea with interrupted plain catgut sutures was accomplished, and in so doing the major portion of the testicular tissue was replaced The tunica vaginalis was then everted and interrupted sutures applied to the cut edges Considerable hematoma was noted within the tissues of the spermatic cord extending well up to the external inguinal ring The scrotal skin was closed with interrupted plain catgut sutures without drainage of the scrotum Postoperatively the patient received penicillin and streptomycin therapy, and an adhesive scrotal support was applied He was afebrile in the postoperative course and was discharged 6 days following admission to the hospital with primary healing of the scrotal wound

Followup examinations over the past 4 years have revealed a complete restoration of the normal size, contour and consistency of the injured testicle and the patient remains asymptomatic

Case 2 A 28-year-old white man was admitted to the Jewish General Hospital June 19, 1956, with a history of having struck himself on the right testicle while walking to the bathroom during the night He was admitted to hospital 6 hours following the injury, complaining of excruciating pain in the right testicle and marked swelling of the right side of the scrotum His past history was noncontributory Examination revealed a well developed and well nourished patient lying flat in bed and complaining of intense pain in the right side of the scrotum He exhibited marked pallor The blood pressure was 120 over 80 millimeters of mercury Pulse was 70 per minute Temperature was 98.2 degrees Examination of the scrotal contents revealed a hard, tender mass in the right side of the scrotum, approximately twice the normal size of the right testicle It was impossible to differentiate testis from epididymis Pain was markedly accentuated on elevation of the scrotal contents The left testicle and epididymis appeared normal The tentative diagnosis was traumatic hematocele, on the right side

Urinalysis showed 1 to 3 red blood cells and 3 to 8 white blood cells per high power field The white blood count was 8900 per cubic millimeter, hemoglobin was 16 6 gm per cent Exploration of the scrotum was carried out within one-half hour following admission to hospital An incision was made through the right anterior surface of scrotum, the tunica vaginalis was opened and a small amount of clear, straw-colored fluid was noted The right testis was found to be markedly enlarged and there appeared to be a considerable increase in tension within the tunica albuginea and a bluish decoloration was noted An incision was made into the anterior aspect of the testis through the tunica albuginea and immediately an old blood clot protruded through the opening

A small portion of the testis was found to be necrotic and a debridement was carried out Good hemostasis was obtained after the blood clot was removed, and the tunica albuginea was then sutured without creating undue tension within the testicle The tunica vaginalis was then everted and sutured and a small Penrose drain was inserted into the scrotal opening and the skin closed around it An adhesive scrotal suspensory was applied

The pathological diagnosis of the portion of testicular tissue removed was "fragments of testicular tissue the seat of edema and hemorrhage" The patient received chloromycetin postoperatively and was discharged from hospital on the sixth postoperative day with the wound well healed

He has been examined at monthly intervals for the past 4 months There is no apparent diminution in the size of the testicle as compared with the contralateral side and the contour and consistency appear normal He remains completely asymptomatic

DISCUSSION

In a thorough review of the literature, McCrea was able to collect 12 cases of rupture of the testicle, to which he added another of his own All injuries were due to direct impact on the testicle by a sudden severe force Of the cases reviewed an orchiectomy was performed in eight instances, suture of the tunica albuginea in 3 cases, and a "bottle operation" (eversion of tunica vaginalis) in 2 cases As examples of the nature of the accident involved, the following were noted struck with baseball, kicked by horse, struck by sledge hammer, struck in scrotum while playing baseball, fell astride metal handrail He concluded from an analysis of the cases presented that the scrotum should be surgically opened and the testicle examined in every instance in which there is a history of trauma and a diagnosis of hematocele is made

Dundon reported a case of rupture of the testicle following a kick in the scrotum Exposure 8 hours following injury revealed a longitudinal rupture of the tunica albuginea with protrusion of the testicular tissue The tunica albuginea was closed with interrupted sutures

Land reported a case of closed rupture of the testicle, in a 16-year-old boy who received the full impact of a soccer ball kicked by a player standing about one foot away Symptoms appeared 2 days following injury and exploration revealed an anterior tear one and a half inches long on the anterior surface of the tunica albuginea A conservative debridement was carried out and the tunica albuginea sutured, with good result He advocates exploration of recently traumatized testicles where there is much local pain and swelling, also pointing out that evacuation of the hematocele is itself valuable

Norton, et al , Trabucco, et al , and Long have reported cases of closed rupture of the testicle Norton's case concerned a 34-year-old man who was in an automobile accident and sustained injury to the scrotum and multiple fractures of the extremities Exploration of the scrotum revealed clotted blood within the tunica vaginalis, multiple lacerations of the tunica albuginea and complete rupture of the lower two-thirds of the testicle Orchiectomy was performed Long reported on a 32-year-old naval petty officer who was thrown from a motorcycle and developed severe pain and swelling of the scrotum He displayed signs of mild shock Exploration revealed distension of the tunica vaginalis with blood, and evacuation of testicular tissue and blood clot revealed an empty shell of tunica albuginea laid open by a long vertical wound Orchiectomy was performed

Cassie recently reported an unusual case, in which a young man, aged 22, suffered a painless rupture of his left testis from a trivial injury Exploration revealed a testis of almost normal size split down its anterior aspect, and the sac full of apparently normal extruded testicular contents The testis was sutured and a biopsy taken, which showed malignant tumor, probably seminoma A chest x-ray revealed metastases in the lungs, and an orchiectomy was subsequently performed

Severe pain and swelling in the scrotum, nausea and vomiting, and varying degrees of shock, form the clinical picture in cases of rupture of the testicle It is noted that contusions of the testicle without rupture present a more severe degree of shock than those with a rent in the tunica albuginea and eventration of the testicular tissue In analyzing the cases described in the literature it is apparent that salvage of the testis could only be accomplished by early surgical exploration of the injured organ In those cases where delayed exposure was carried out, orchiectomy was the usual procedure adopted

Analysis of the cases would indicate several possible methods of surgical repair of the ruptured testicle

Incision of the tunica albuginea with release of blood clot and necrotic tissue, where there is obvious increase in tension within the tunica albuginea, e g , case 2

Suture of the ruptured tunica albuginea and ligation of testicular bleeders e g , case 1

Eversion and suture of the tunica vaginalis where the tunica albuginea cannot be closed over protruding testicular tissue

Orchiectomy in cases of severe rupture of the tunica albuginea and massive disorganization of the testicular tissue

SUMMARY

Two cases of rupture of the testicle without penetrating wounds of the scrotum are added to the 19 cases reported in the world literature

The clinical picture and surgical methods employed in repairing the testicle are described

Evidence from our own cases and those reviewed in the literature would indicate that early surgical exposure of the scrotum in cases following trauma to the testicle where a diagnosis of hematocele is made, will result in salvage of many testes otherwise doomed to complete atrophy

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CARCINOMA OF THE PROSTATE WITH SIMULTANEOUS BILATERAL TESTICULAR METASTASES CASE REPORT WITH SPECIAL STUDY OF ROUTES OF METASTASES

DWAYNE E HOWARD, WAYLAND K HICKS AND E W SCHELDRUP

Metastases from carcinoma of the prostate spread by local extension, and by way of the lymphatics and bloodstream [1] Their incidence is usually found in one-third to one-half of cases The sites involved vary greatly In 176 cases Arnheim[2] at autopsy reported the distribution of metastatic lesions as follows lymph nodes 176, bones 46, lungs 22, liver 22, pleura 15, adrenals 13, kidneys 6, peritoneum 5, spleen 5, skin 4, pancreas 3, brain 3, vena cava 2, stomach 2, small intestine 2, and one each in colon, mesacolon, portal vein and gallbladder

The incidence of metastases from carcinoma of the prostate to the testicle is extremely rare In a series of 5000 autopsies, Klinger[3] found 142 with secondary tumors in the genitourinary tract of which three involved the testicle, one a lymphoma, one from the stomach and the other from a teratoma of the testes (?) but none from carcinoma of the prostate Abeshouse and his group[4] in their recent thorough and excellent article dealing with bilateral tumors of the testicles collected from the literature 5 cases of unilateral metastases of carcinoma of the prostate to the testicle My perusal of the literature has shown that the first case was reported by Semans in 1938,[5] the second by Helfert and Pinck in 1944,[6] the third case by Baird and Hare in 1948,[7] the fourth case by Bradham in 1950,[8] and the fifth case by Ivan Potts, Sydney, Australia in 1953 [9] Kay, Hennigan and Hooper reported three additional cases in 1954 [10] Arduino reported an additional case in 1955 [11] To my knowledge there are no reports of bilateral metastases to the testicles from carcinoma of the prostate I would like to present the following case whose features seem to fit into that category

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Read at annual meeting, North Central Section of American Urological Association, Cleveland, Ohio, October 3–5, 1956

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[2] Arnheim, F K Carcinoma of prostate J Urol , 60 599, 1948

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[5] Semans, J H Carcinoma of prostate with metastases in testes J Urol , 40 524–529, 1938

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[11] Arduino, L J Unusual metastases of carcinoma of the prostate with report of four cases Am Surg , 21 1146–1153, 1955

CASE REPORT

SV11604 G G, an 81-year-old white man, was admitted to the hospital June 4, 1952 with the complaint of frequency of urination of 6 weeks' duration He had diuria of very half hour and nocturia of 6 to 8 times In addition his appetite had been poor and he had lost some weight He was weak and mentally cloudy, but responsive and co-operative The residual urine was 950 cc

The past history, family history and systemic review were not pertinent The physical examination disclosed an ill man The blood pressure was 170/80 The heart was fibrillating The lower abdomen was distended The genitalia were normal to appearance and palpation The rectal examination disclosed a firm, rubbery prostate 1 to 2 plus enlarged, not fixed and without nodularity The laboratory studies revealed blood urea nitrogen of 132 mg per cent, mild leukocytosis but no anemia The urine specimen contained numerous pus cells and 3 plus albumin An acid phosphatase determination was not done

Three weeks after admission, the patient having been on indwelling Foley catheter drainage and supportive treatment, his blood urea nitrogen was 19 6 mg per cent At this point a transurethral prostatic resection with bilateral vasectomy was done, 50 0 gm tissue was removed The pathological report was carcinoma of the prostate (fig 1) His hospital course was uneventful and he was discharged 8 days following surgery voiding satisfactorily Diethylstilbestrol, 5 mg t i d was prescribed

The patient failed to return for followup examinations He took the initial

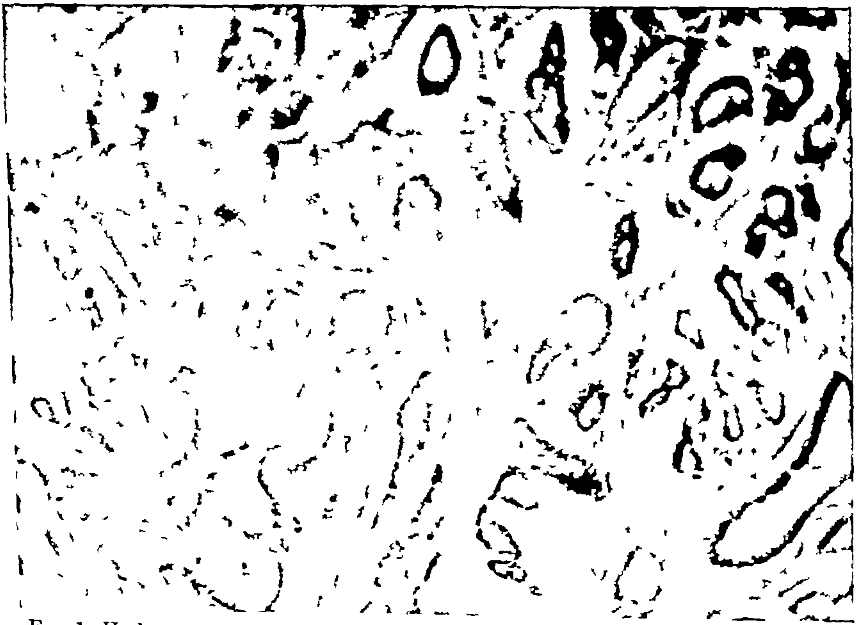

FIG 1 High power photomicrograph Section of original prostatic tissue, 1952

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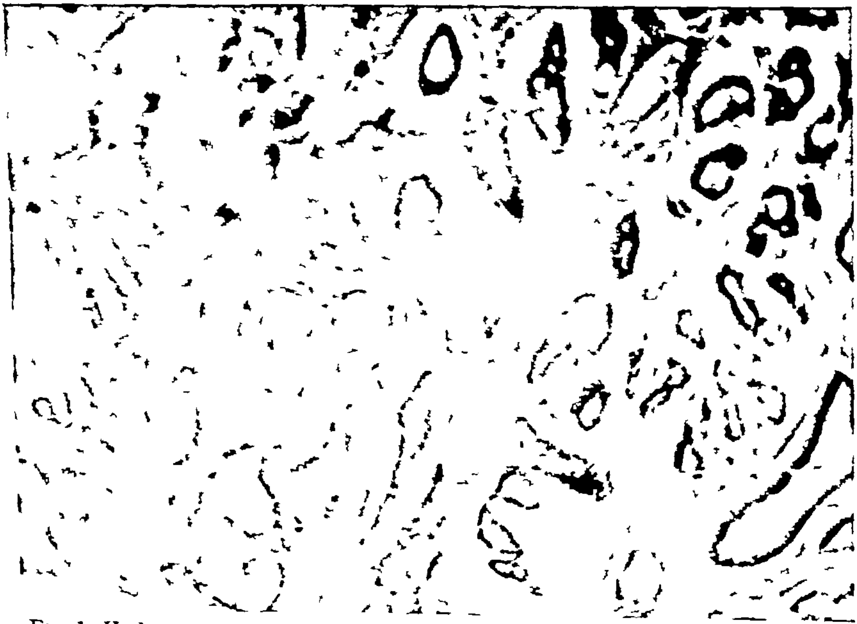


Fig 1 High power photomicrograph Section of original prostatic tissue 1952

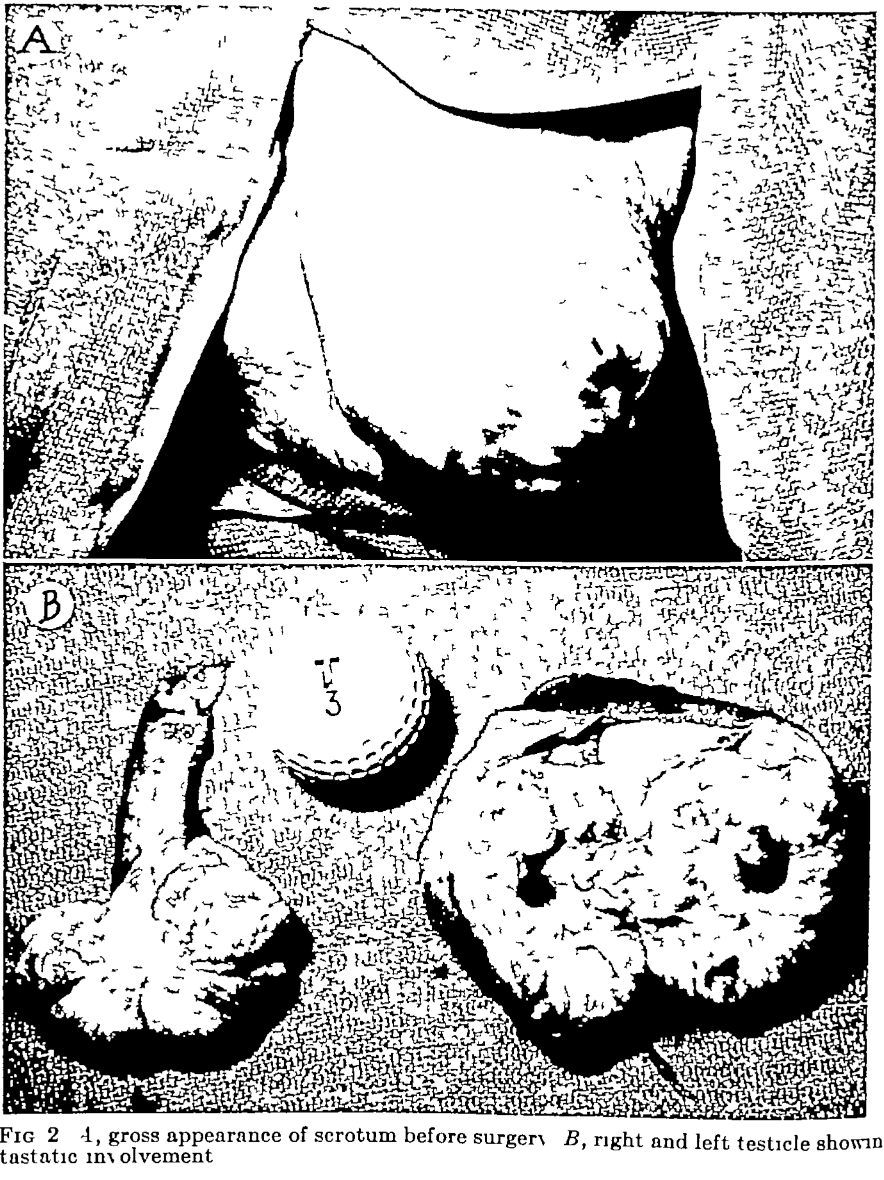


FIG 2 *A*, gross appearance of scrotum before surgery *B*, right and left testicle showing metastatic involvement

supply of estrogens but none thereafter He was hospitalized August 23, 1955 again in urinary retention His blood urea nitrogen was 19 6 mg per cent The general physical examination was unchanged except for the scrotal findings There were enlarged masses in both sides of the scrotum (fig 2, *A*) On the left there was induration with the mass fixed to the skin, this mass was hard, slightly irregular, nontender and about 10 by 15 cm in size On the right the mass was smaller, 8 by 10 cm , also hard, irregular, and nontender Rectal examination revealed the prostate to be hard, irregular, fixed and about 2 plus enlarged, with extension into both seminal vesicles

On August 24, 1955 a cystolithotripsy, transurethral prostatic resection and bilateral orchiectomy were done, 31.0 gm. typically malignant prostatic tissue was removed.

Pathological examination of the tissue revealed the following. The speci-

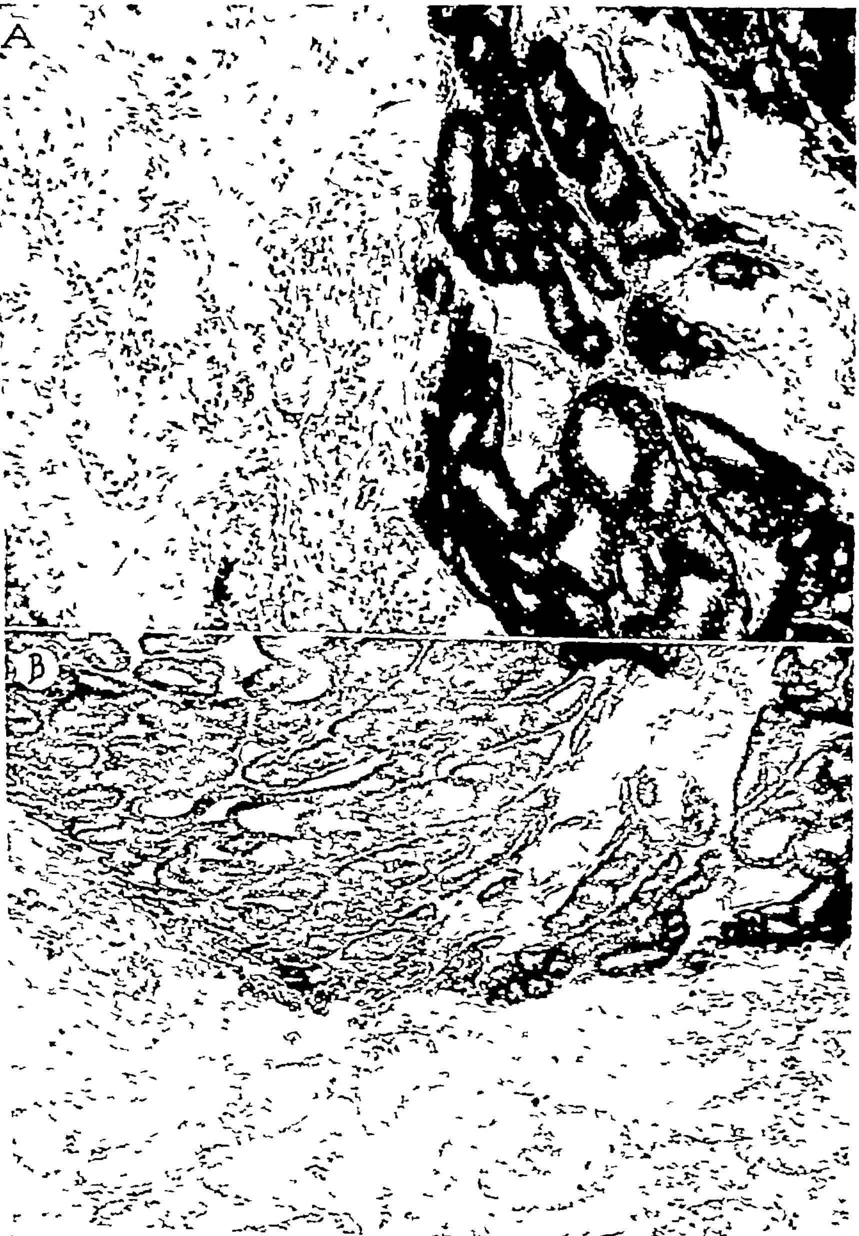
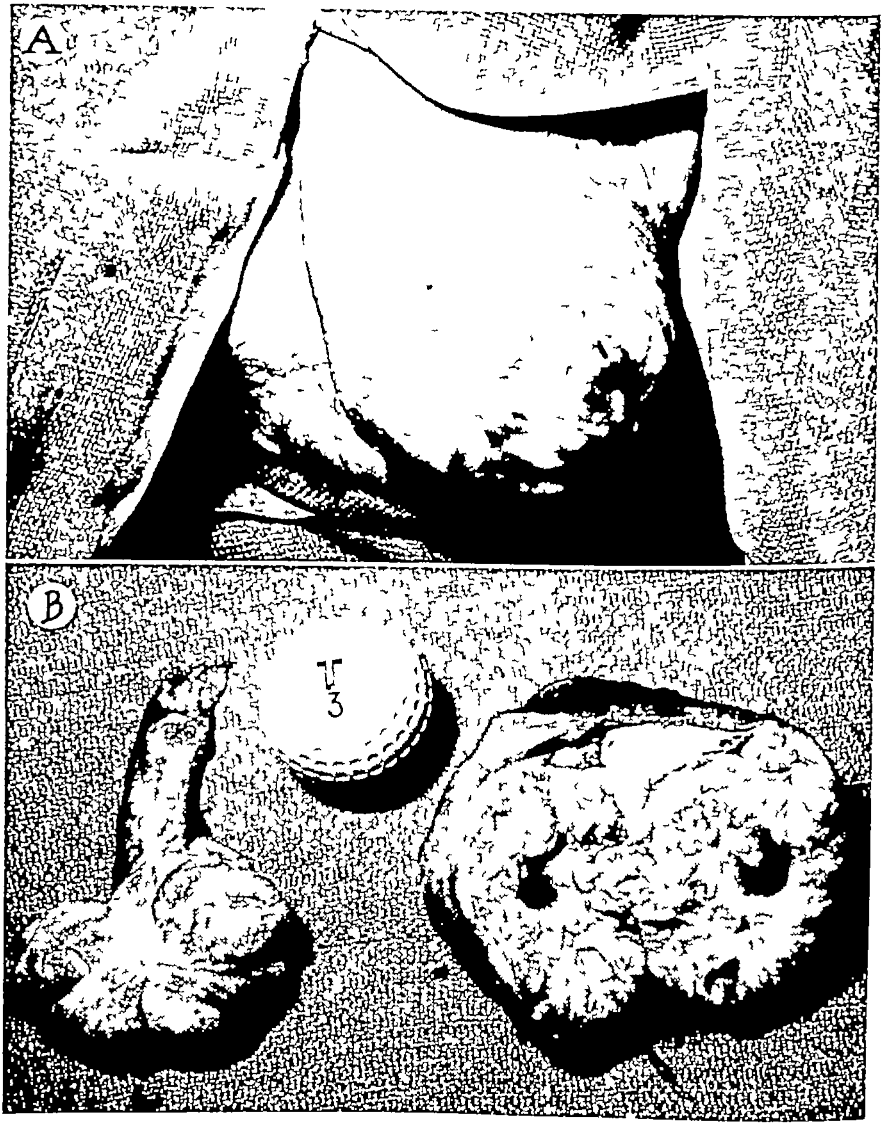


Fig. 3. Low power photomicrograph. Sections from tumor area of right and left testicle



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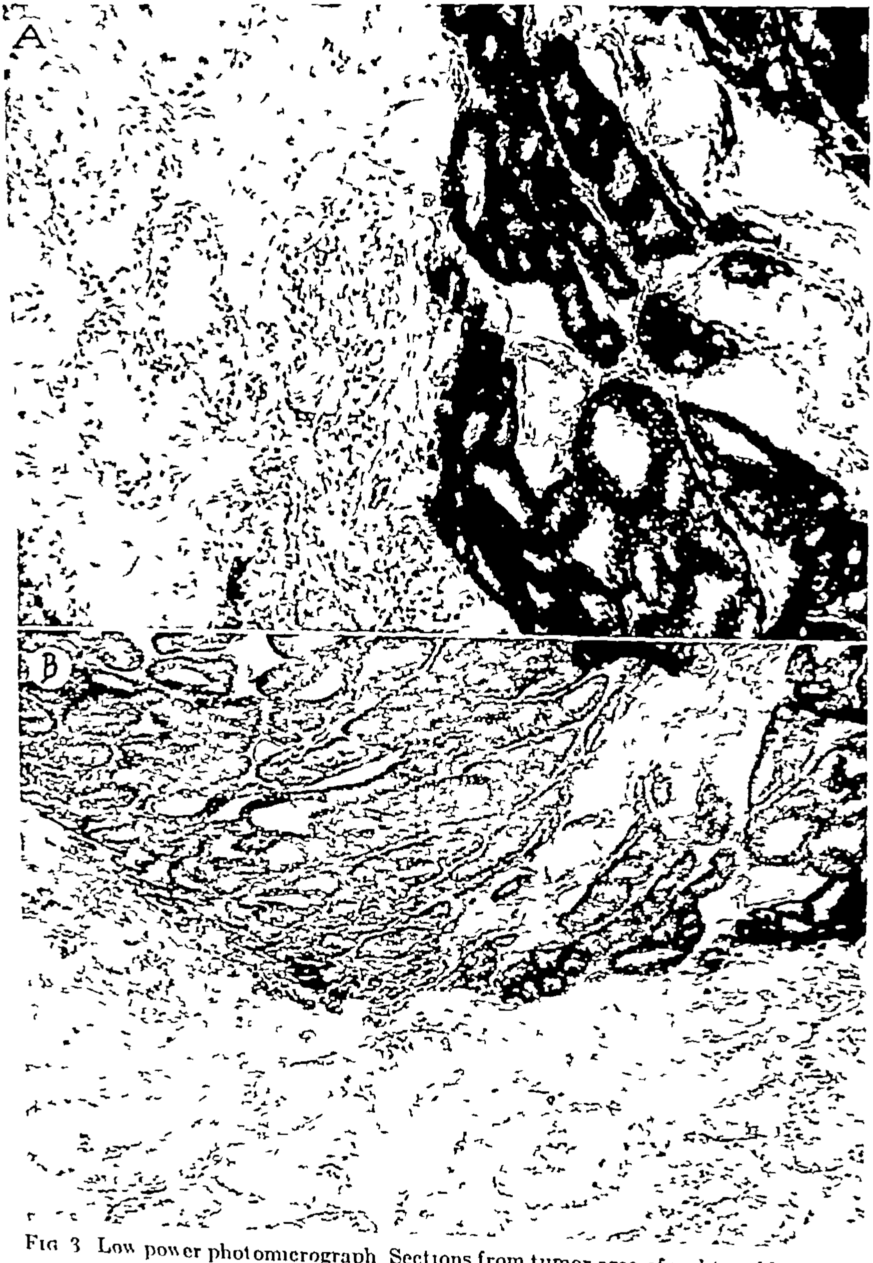

Fig 3 Low power photomicrograph Sections from tumor area of right and left testicle

men consisted of both testicles, and a portion of each cord (*fig 2, B*) One testicle measured 6 by 4 by 5 cm and contained a nodular tumor measuring 3 cm in diameter The tumor was soft and gray in color The other testicle measured 4 by 2 by 2½ cm The body showed some hemorrhage Attached to and involving the testicle was a large, coarsely lobulated tumor that measured 7½ cm in the greatest diameter The tumor was soft and yellowish-gray in color Microscopically one testicle showed a tumor made up of hyperchromatic epithelial cells infiltrating in gland-like structures The tumor attached to the cord and involving the other testicle showed the same structures See figure 3

Followup examination September 18, 1956, revealed a healthy white man The prostate was small rectally, with minimal firmness in the right lobe and seminal vesicle There was fixation on the right The acid phosphatase was within normal limits No demonstrable metastases were found in the chest or in the bony pelvis or lumbar spine, and no evidence of local recurrence of malignancy in the scrotum

DISCUSSION

It has been our good fortune to have the help of Dr E W Scheldrup, associate professor of anatomy at the College of Medicine, State University of Iowa, in the preparation of this paper The following information prepared by Dr Scheldrup as to routes of metastases from prostate gland to testes is presented

A) *Retrograde venous route* The following two anatomic routes are possible

1) Prostatic venous plexus to internal iliac (hypogastric) vein thence to inferior vena cava Malignant cells would then have to ascend the inferior vena cava to the origin of the right internal spermatic vein and pass in a retrograde direction to the right testis On the left side, cells would have to first enter the left renal vein and then pass in a retrograde direction to the left testis

2) Prostatic venous plexus directly posterior to the inferior hemorrhoidal vein and hemorrhoidal plexuses and thence to the scrotum via scrotal branches of the internal pudendal veins which are in communication with the inferior hemorrhoidal veins and hemorrhoidal plexuses

Both of these venous routes are highly speculative in the absence of actual demonstration at autopsy of the venous pathways involved The cases of venous metastasis to the testis (left) that have been described have almost uniformly been secondary to tumors of the left kidney

B) *Arterial embolism* The pathway here, of course, would have to be as follows Prostatic venous plexus to hypogastric vein to inferior vena cava to heart, thence through pulmonary circulation with return to heart and out into the systemic circulation and ultimately to the testes via the internal spermatic arteries The proven cases of this route have shown rather widespread metastases in other parts of the body[12] In the absence of metastases elsewhere and without histologic demonstration of actual arterial embolism in the terminal portions of the internal spermatic artery this route seems unlikely in the case presented

[12] Willis, R A The Spread of Tumors in the Human Body London Butterworth & Co, Ltd, 1952

here However, Semans[5] reported a case in which testicular metastasis probably occurred by way of the arterial route since he was able to demonstrate arterial embolism Moreover, widespread metastasis is not essential to prove the arterial route, for Graves and Militzer[13] cite a case of solitary metastasis from prostate to thyroid, and Mintz and Smith,[14] in reviewing 100 cases of prostatic cancer cite such rare locations for metastasis as brain, spinal cord, eye, pancreas, gallbladder, pericardium, adrenal, diaphragm, penis and skin Helfert and Pinck attributed their case of unilateral testicular metastasis to arterial embolism [6] Their evidence for this conclusion is nil and highly speculative

C) *Retrograde lymphatic route* Although metastasis from the prostate is said to be much more common by the bloodstream than by lymphatics, lymphatic metastasis does occur and in this particular case has more scientific backing than bloodstream metastasis Two routes are possible, as follows

1) In 1904 Bruhns,[15] by means of injection experiments, demonstrated lymphatic connections between the prostate and epididymis and testis in man by way of periductal lymphatics on the vas deferens Injection of prostatic lymphatics thus showed spread in a retrograde direction to *both testes* Furthermore there is cross lymphatic anastomoses between the two halves of the scrotal sac which is said to account for the metastasis of a primary testicular tumor to the opposite testis [12] Thompson and Pilcher[16] described the first case of extension of cancer of the prostate along the vas to the testes Humphrey[17] described a similar case Although in these cases the vas and epididymis were the seat of metastasis, there is no reason why the process could not either have progressed to the testes directly or extended to them from the terminal vas and epididymis This possible and very probable route of metastasis raises a very interesting point regarding the advisability of more radical surgery in those cases of prostatic cancer which are subjected to bilateral orchiectomy If, indeed, periductal lymphatics on the vas are responsible for at least some cases of metastasis to the testes then it would seem as ill advised to leave the vas intact as it is to do a subtotal hysterectomy for carcinoma of the uterine body—the vas like the cervix may be a site of future disease and inasmuch as it is rendered functionally useless one might consider its complete excision

2) Lymphatics from the prostate drain to the hypogastric lymph nodes, thence to the common iliac nodes and thence to the lateral and preaortic nodes situated retroperitoneally in the abdominal cavity The testes drain directly to the lateral and preaortic nodes It is conceivable that via this pathway one may have retrograde extension to the testes Only the finding of involvement of the nodes in question could verify the point, however This route seems unlikely in

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[16] Thompson, G J and Pilcher, F Carcinoma of the vas deferens J Urol, 34 714–717, 1935

[17] Humphrey M A Metastases in the epididymis from cancer of the prostate Case report J Urol, 51 641–642 1944

men consisted of both testicles, and a portion of each cord (fig 2, *B*) One testicle measured 6 by 4 by 5 cm and contained a nodular tumor measuring 3 cm in diameter The tumor was soft and gray in color The other testicle measured 4 by 2 by 2½ cm The body showed some hemorrhage Attached to and involving the testicle was a large, coarsely lobulated tumor that measured 7½ cm in the greatest diameter The tumor was soft and yellowish-gray in color Microscopically one testicle showed a tumor made up of hyperchromatic epithelial cells infiltrating in gland-like structures The tumor attached to the cord and involving the other testicle showed the same structures See figure 3

Followup examination September 18, 1956, revealed a healthy white man The prostate was small rectally, with minimal firmness in the right lobe and seminal vesicle There was fixation on the right The acid phosphatase was within normal limits No demonstrable metastases were found in the chest or in the bony pelvis or lumbar spine, and no evidence of local recurrence of malignancy in the scrotum

DISCUSSION

It has been our good fortune to have the help of Dr E W Scheldrup, associate professor of anatomy at the College of Medicine, State University of Iowa, in the preparation of this paper The following information prepared by Dr Scheldrup as to routes of metastases from prostate gland to testes is presented

A) *Retrograde venous route* The following two anatomic routes are possible

1) Prostatic venous plexus to internal iliac (hypogastric) vein thence to inferior vena cava Malignant cells would then have to ascend the inferior vena cava to the origin of the right internal spermatic vein and pass in a retrograde direction to the right testis On the left side, cells would have to first enter the left renal vein and then pass in a retrograde direction to the left testis

2) Prostatic venous plexus directly posterior to the inferior hemorrhoidal vein and hemorrhoidal plexuses and thence to the scrotum via scrotal branches of the internal pudendal veins which are in communication with the inferior hemorrhoidal veins and hemorrhoidal plexuses

Both of these venous routes are highly speculative in the absence of actual demonstration at autopsy of the venous pathways involved The cases of venous metastasis to the testis (left) that have been described have almost uniformly been secondary to tumors of the left kidney

B) *Arterial embolism* The pathway here, of course, would have to be as follows Prostatic venous plexus to hypogastric vein to inferior vena cava to heart, thence through pulmonary circulation with return to heart and out into the systemic circulation and ultimately to the testes via the internal spermatic arteries The proven cases of this route have shown rather widespread metastases in other parts of the body[12] In the absence of metastases elsewhere and without histologic demonstration of actual arterial embolism in the terminal portions of the internal spermatic artery this route seems unlikely in the case presented here However, Semans[5] reported a case in which testicular metastasis probably occurred by way of the arterial route since he was able to demonstrate arterial embolism Moreover, widespread metastasis is not essential to prove the arterial route, for Graves and Militzer[13] cite a case of solitary metastasis from prostate to thyroid, and Mintz and Smith,[14] in reviewing 100 cases of prostatic cancer cite such rare locations for metastasis as brain, spinal cord, eye, pancreas, gallbladder, pericardium, adrenal, diaphragm, penis and skin Helfert and Pinck attributed their case of unilateral testicular metastasis to arterial embolism [6] Their evidence for this conclusion is nil and highly speculative

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[12] Willis, R A The Spread of Tumors in the Human Body London Butterworth & Co, Ltd, 1952

C) *Retrograde lymphatic route* Although metastasis from the prostate is said to be much more common by the bloodstream than by lymphatics, lymphatic metastasis does occur and in this particular case has more scientific backing than bloodstream metastasis Two routes are possible, as follows

1) In 1904 Bruhns,[15] by means of injection experiments, demonstrated lymphatic connections between the prostate and epididymis and testis in man by way of periductal lymphatics on the vas deferens Injection of prostatic lymphatics thus showed spread in a retrograde direction to *both testes* Furthermore there is cross lymphatic anastomoses between the two halves of the scrotal sac which is said to account for the metastasis of a primary testicular tumor to the opposite testis [12] Thompson and Pilcher[16] described the first case of extension of cancer of the prostate along the vas to the testes Humphrey[17] described a similar case Although in these cases the vas and epididymis were the seat of metastasis, there is no reason why the process could not either have progressed to the testes directly or extended to them from the terminal vas and epididymis This possible and very probable route of metastasis raises a very interesting point regarding the advisability of more radical surgery in those cases of prostatic cancer which are subjected to bilateral orchiectomy If, indeed, periductal lymphatics on the vas are responsible for at least some cases of metastasis to the testes then it would seem as ill advised to leave the vas intact as it is to do a subtotal hysterectomy for carcinoma of the uterine body—the vas like the cervix may be a site of future disease and inasmuch as it is rendered functionally useless one might consider its complete excision

2) Lymphatics from the prostate drain to the hypogastric lymph nodes, thence to the common iliac nodes and thence to the lateral and preaortic nodes situated retroperitoneally in the abdominal cavity The testes drain directly to the lateral and preaortic nodes It is conceivable that via this pathway one may have retrograde extension to the testes Only the finding of involvement of the nodes in question could verify the point, however This route seems unlikely in

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[13] Graves, R C and Militzer, R E Carcinoma of the prostate with metastases J Urol, 33 235–251 1935

[14] Mintz E R and Smith, G G Autopsy findings in 100 cases of prostatic cancer New Engl J Med 211 479–487 1934

[15] Bruhns, C Untersuchungen über die Lymphgefasse und Lymphdrusen der Prostata des Menschen Arch f Anat u Entwick, Geschichte, pp 330–349, 1904

[16] Thompson, G J and Pilcher, F Carcinoma of the vas deferens J Urol, 34 714–717, 1935

[17] Humphrey M A Metastases in the epididymis from cancer of the prostate Case report J Urol 51 641–642 1944

the present case One cannot ignore the fact, though, that this route has been taken in most recorded cases of metastasis to the testis from gastrointestinal and retroperitoneal malignancies [12]

D) *Intraductal route in the vas deferens* To my knowledge, no one has commented on this great potential route and it has certain features to recommend it First of all, after operation malignant cells from the prostate would have relatively easy access to it Secondly, whole tumor cells (at least in animal experimentation) are not required for successful metastasis and cancer invoking material (virus? for lack of a better term) can bring about successful implants and transplants when in very fluid and dispersed state This places metastatic material in much the same category as infected urine for which vasectomy is performed to prevent epididymitis in some cases of prostatic resection In addition, malignant cells from the prostate may grow by extension intramurally along the vas to the testis This was the route in the case of Thompson and Pilcher[16] and they erroneously attributed it to retrograde lymphatic extension even though, on microscopic examination, there was found a layer of tissue of the same cellular structure as that removed from the prostate contiguous with the muscular layer of the vas and in an intramural position therefore Perhaps this occurs more often than suspected and would suggest the advisability of more radical surgery with respect to the vas

SUMMARY

A rare and interesting case of carcinoma of the prostate with simultaneous metastases to both testicles is reported Some pertinent information from the literature is also presented We are unable, with the information at hand, to outline the route of metastases in this case

Grateful acknowledgment is herewith made to Dr A C Starry, Dr James Brown and Dr Arne Knutsen, pathologists, for their valuable help

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GENITAL TUBERCULOSIS IN THE MALE CLINICAL PATHOLOGY AND EFFECT ON FERTILITY

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All urologists are at some time confronted with the problem of genital tuberculosis in the male The clinical pathology of the disease, its effect on fertility and the most up-to-date treatment are subjects of much discussion

The fertility status of 60 patients with genital tuberculosis was recently studied at the Research Unit for Genito-Urinary Tuberculosis, Veterans Administration Hospital, Bronx, New York City The pathological changes of genital tuberculosis were correlated with the semen analyses and the fertility indices of the patients Current treatment regimens were evaluated Positive cultures or pathological specimens were required as proof of the disease

CLINICAL PATHOLOGY OF GENITAL TUBERCULOSIS

Most male patients with renal tuberculosis eventually develop genital involvement (Medlar, Nesbit) Conversely, every man with genital tuberculosis should be examined repeatedly for a tuberculous renal lesion

The dangers from genital tuberculosis are fourfold

1) Contracture of the bladder may result from continuous spillage of tuberculous material from the prostate

2) Disabling symptoms may result from urethral irritation

3) Draining sinuses or fistulas of the scrotum or perineum may occur

4) Genital tuberculosis may conceivably be a focus for the dissemination of fatal miliary or meningeal tuberculosis and should therefore be eradicated if possible (Moore, Simmonds, Lehmann, Medlar, Menville)

We are unable to contribute conclusively to the perennial academic debate as to whether most genital tuberculosis descends directly from the kidneys by contamination, via the infected urine, or is hematogenic (hemic) from the original pulmonary or intestinal focus Fifty-one of our genital cases (85 per cent) appeared to have been infected by the urine from tuberculous kidneys Nine cases (15 per cent) showed no clinical evidence of renal lesions either by x-ray or ureteral culture In these 9 cases the disease was limited to the genital organs as far as could be determined, and the positive urine cultures were assumed to come from the tuberculous prostates However, 58 per cent of our epididymal lesions showed no thickening or nodularity of the vas This failed to support the view that the infection descends the vas in every case It appeared probable to us that the genital tract could be infected either by urinary contamination from the infected kidneys, or by hematogenous spread directly to the genitalia, but that urinary contamination was much more common

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Thirty-two (54 per cent) of the 60 cases gave a history of a recognized, active, extra-genitourinary tuberculous process. There were 22 cases (36 per cent) with histories of active pulmonary tuberculosis with an average time interval of about five years (4.83 years) between the diagnosis of pulmonary tuberculosis and the onset of genitourinary tuberculosis. Seventeen cases (28.3 per cent) gave a history of bone tuberculosis in addition to genitourinary tuberculosis. No time relationship could be established, since just as many cases developed after, as before the genitourinary tuberculosis. This supports the current view that the initial lesion is pulmonary, with hematogenic (hemic) spread to bones and kidneys.

The diagnosis of *prostatic tuberculosis* was made by a correlation of rectal

TABLE 1 *Summary of genital findings*

	Per Cent	Cases
Number of cases of prostatic tuberculosis	71	43
Number of cases of dilated prostatic ducts	88.3	53
Number of cases of seminal vesicle involvement	31.7	19
Number of cases of epididymal nodules (bilateral 9)	41.7	25
Number of cases of epididymectomy (bilateral 3)	38.3	23
Number of cases of orchiectomy and epididymectomy (bilateral 1)	3.1	2
Number of cases of vas thickened and nodule (bilateral 4)	18.3	11
Total cases of genital tuberculosis	100	60

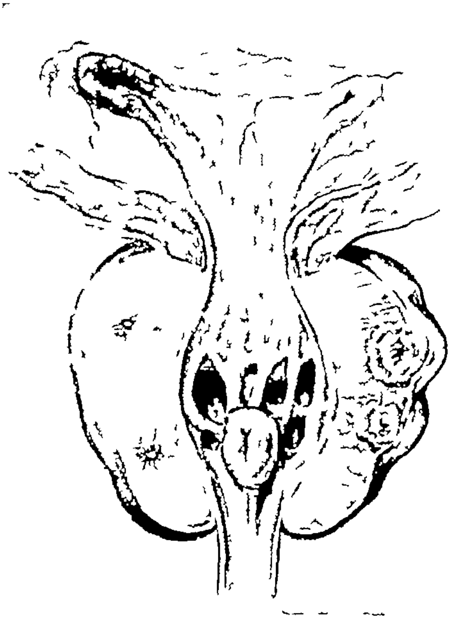


FIG 1 Appearance of tuberculous prostate and dilated prostatic ducts as seen on urethroscopy in prostatic urethra. These dilated ducts result from extensive fibrosis associated with chronic inflammatory process.

findings, positive semen cultures, pus cells in the semen, dilated prostatic ducts, cavities shown by urethrograms, and calcification in x-ray studies Prostatic smears were not used in diagnosis since a miliary spread of the disease from massage was a possibility

The prostate was obviously involved in 71 per cent (43 cases) of the 60 genital tuberculosis cases studied, and in an even greater number, 88 per cent (53 cases), dilated prostatic ducts were observed in the posterior urethra Contrary to popular teaching there was no "characteristic feel" to these tuberculous prostates Some were small and fibrotic, some were soft, where caseous centers had sloughed out, and some were granular Only 25 per cent presented frank nodules Many had firm ridges paralleling the course of the ejaculatory ducts

Figures 1 to 3 illustrate the pathology of prostatic tuberculosis by urethrography

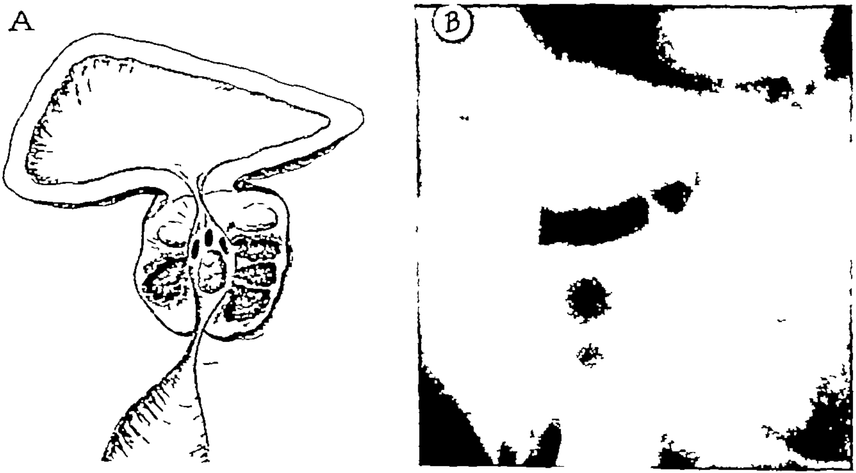


FIG 2 A, dilated prostatic ducts often communicate with cavities in tuberculous prostate, as illustrated in drawing *B*, these ducts and cavities are filled on urethrography

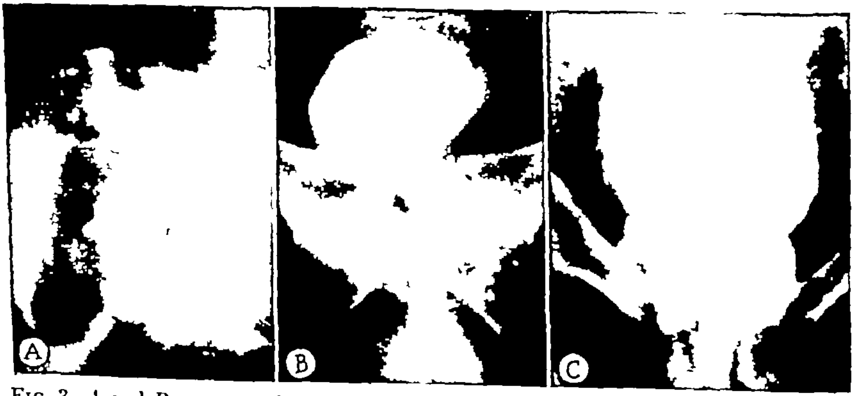


FIG 3 *A* and *B* cystourethrograms show cavities in prostate *C*, at times entire prostate will slough out leaving large fore bladder or *vorblase* At times this will progress into urethrocolic fistula or perineal fistula

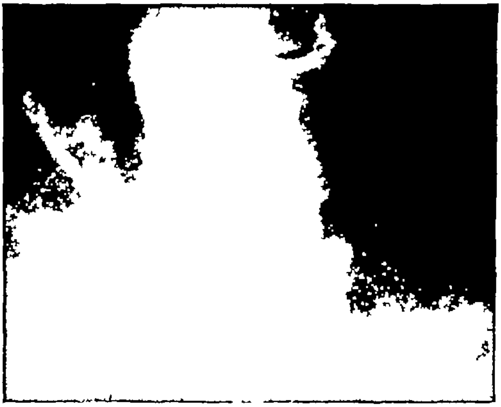


FIG 4 Firm, enlarged and irregular seminal vesicles at times showed calcifications by x ray

Dilated prostatic ducts In forty-one (97 per cent) of the 43 cases with palpable prostatic involvement, and in fifty-three (88 per cent) of the sixty genital tuberculosis cases studies, dilated prostatic ducts were observed in the posterior urethra The ducts were located on the floor of the prostatic urethra just proximal to the verumontanum and were not to be confused with the ejaculatory ducts which were located on the verumontanum In acute prostatic urethritis, the prostatic urethra was fiery red and edematous, velvety folds were found on the urethral floor In less acute cases the prostatic urethral floor appeared trabeculated, with longitudinal ridges radiating from the verumontanum In more chronic cases the prostatic ducts were dilated and at times "golf-hole" in appearance, resembling small diverticula In some cases a flocculent exudate was noted coming from the ducts The ducts were best visualized with the right angle lens, early in the cystoscopic procedure, before irritation by the instrument could cause reddening of the urethral floor and bladder neck spasm

It was recognized that dilated prostatic ducts were not specific for tuberculosis However, the frequent occurrence of dilated ducts in the cases with known prostatic tuberculosis justified the suspicion of prostatic involvement when they were seen in patients with renal or epididymal tuberculosis Tuberculosis was suspected in these men even when no nodules were palpable in the prostate All cases in which large ducts were noted were suspected of having tuberculosis and a search for the organisms was made

In a pathological study, R A Moore concluded that the prostate was involved in 75–90 per cent of cases of genitourinary tuberculosis In our series 71 7 per cent (43 cases) were diagnosed clinically as tuberculous prostatitis, by palpation and correlation, and 88 3 per cent (53 cases) showed dilated prostatic ducts These clinical figures correspond closely with those obtained from Dr Moore's pathological study

The ducts can be filled by urethrography and cavities in the prostate outlined (figs 2 and 3) In active tuberculous prostatitis large caseous areas may coalesce, liquefy, and slough out Occasionally, the entire contents of the prostatic capsule may slough leaving a large cavity or fore-bladder (*vorblase*) as illustrated by two of our cases The abscess may rupture beyond the confines of the prostatic capsule and result in fistula formation or multiple perineal sinuses

Seminal vesicle Involvement was present in 14 per cent (19 cases) At times calcification of seminal vesicles was observed (fig 4)

Epididymal tuberculosis occurred sometime during the course of the disease in 63 per cent (38 cases) of the 60 cases reviewed Adjacent testes were not involved, even in the presence of large epididymal abscesses (fig 5) Only 14 (41 per cent) thickened or nodular ductus deferentes were found among 34 epididymal nodules Thickening and nodularity occurred most often in the acute stage of the epididymal involvement Occasionally (6 cases) epididymal nodules showed calcification on scrotal x-ray (fig 6) With patient in knee-chest position, soft tissue x-ray technique gave very satisfactory films In those cases with calcification, the average duration of epididymal disease was seven years Later operative findings showed that calcification was no indication of complete healing, but only of calcium in necrotic areas of long duration

Table 2 illustrates the high clinical incidence of association of prostatic and epididymal lesions All of the cases with seminal vesicle involvement also had prostatic tuberculosis

The finding of only fourteen (41 per cent) thickened or nodular vasa associated with thirty-four epididymal nodules was lower than expected The lack of thickening occurred even in men who had obvious prostatic tuberculosis This clinical finding was supported by operative specimens in which large, chronically

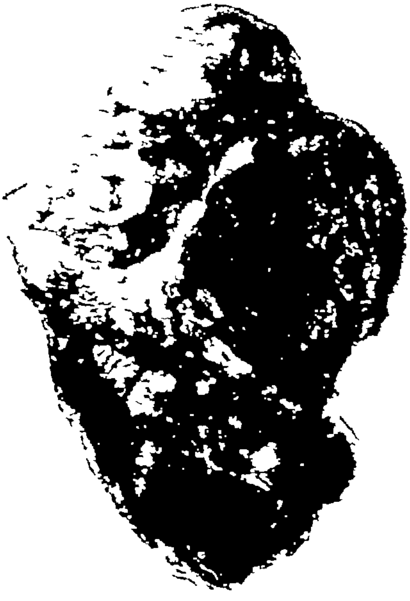


Fig 5 Epididymal tuberculous abscesses rarely involved adjacent testis

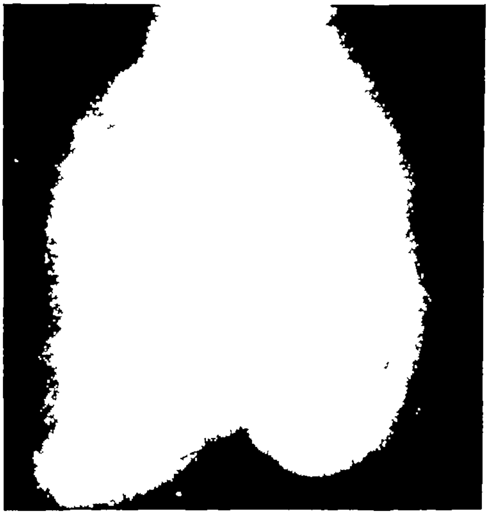


FIG 6 Calcification in some 25 per cent of epididymal nodules was demonstrated by x-rays of scrotum Operative findings showed that calcification was no indication of complete healing, but only of calcium in necrotic areas of long duration

TABLE 2 *Incidence of other genital lesions associated with tuberculous epididymitis (clinical findings)*

	Per Cent	Cases
Total cases of tuberculous epididymitis	63 4	38
Number of cases with associated prostatic tuberculosis	81 6	31
Number of cases with dilated prostatic ducts	86 8	33
Number of cases with seminal vesicle involvement (bilateral 5)	37	14
Number of cases with nodular or beaded vas (bilateral 4)	26 3	10
Number of cases where genital tuberculosis was limited only to epididymis	0	0

inflamed epididymides had attached thin, apparently uninvolved, vasa Sections were routinely taken at various levels along the vas In only one case was a tubercle present in the wall of the vas and this was adjacent to the tail of the epididymis The tubercle was only evident microscopically and no nodule was present The testis itself was uninvolved even in the presence of large abscesses of the epididymis It appeared that M tuberculosis could descend the ductus deferens without causing any thickening

FERTILITY

Our patients with genital tuberculosis asked their doctors two principal questions

1) Was their fertility affected?
2) Would they infect their wives through intercourse?

Most of our patients were sterile, either by the standard of 60 million sperm/cc or by MacLeod's 20 million/cc None were impotent Twenty-three of the men had had children before genital tuberculosis developed However, out of the forty married patients only one child had been born since the diagnosis of genital tuberculosis was made.

Four couples gave histories of miscarriages. Three of these occurred after the diagnosis of genital tuberculosis had been made. Two of these four husbands had no ejaculate by the time we saw them and two of them had very low semen volumes with azoospermia, which unfortunately prevented any study of morphology of the spermatozoa in these patients. In one case there had been three normal pregnancies before the diagnosis of genital tuberculosis. However, following the development of the disease two miscarriages occurred.

There were seventeen childless married men, after 5 to 6 years of marriage. Of this group only five (29 per cent) had sperm in their ejaculate, demonstrating clearly the decrease in fertility. Four of these had sperm despite definite clinical tuberculous involvement on both sides of the prostate and in two cases bilateral epididymal nodules. Three of the five showed dilated prostatic ducts. Of the five who ejaculated spermatozoa all had low semen volumes (1.2, 0.4, 2.0, 1.4, 0.5 cc), low sperm counts and all had poor motility. All five cases fall into the infertile class according to the criteria of Hotchkiss and the revised standards of MacLeod.

Painful ejaculation, described as a throbbing burning sensation at the bulb of the penis or burning along the perineum, was noted by twelve (20 per cent) of the patients. In some dysuria followed ejaculation and two patients had a mucoid urethral discharge for two or three days after ejaculation.

SEMEN ANALYSES

Low semen volume (*table 3*) was a notable feature of prostatic tuberculosis. In 10 patients there was no ejaculate at all and in only 6 cases of prostatic and genital tuberculosis was the semen volume over 2.5 cc.

Semen specimens were collected after 3 days abstinence in clean wide mouthed bottles, from fifty-three of the 60 patients. The 7 patients from whom semen analyses could not be obtained gave no history of having caused a preg-

TABLE 3 *Semen analyses in fifty-three patients with genital tuberculosis* (*low semen volume and inadequate sperm counts were the rule*)

	Per Cent	Cases
No ejaculate	18.8	10
Volume of ejaculate		
1 drop to 0.5 cc	35.8	19
0.5 to 1.0 cc	11.3	6
1.0 cc to 1.5 cc	13.2	7
1.5 cc to 2.5 cc	9.4	5
3 cc to 6 cc	11.3	6
Azoospermia	32.0	17
Oligospermia	20.7	11
Normal count per cc but with very low volume (below 1 cc)	7.5	4
Normal count per cc but low volume (below 2 cc)	13.2	7
Normal analysis by count and volume *alone*	7.5	4

nancy Of the fifty-three examined by semen analysis, only one patient (65 0 mil/cc motility normal 4 0 cc vol) had a relatively normal analysis based on all criteria of the number of sperm, motility and volume In this patient with renal tuberculosis, only large dilated prostatic ducts were noted

PH of the semen was not appreciably altered Most specimens were alkaline, ranging from pH 7 4 to 8 4 In one case with advanced genital tuberculosis with perineal sinuses, azoospermia, and a 1 0 cc volume, an abnormally low pH of 6 9 was recorded

Viscosity was decreased in the 28 cases with azoospermia and oligospermia Thirteen patients had normally viscid semen and in eleven the viscosity was increased There seemed to be no definite relationship between the activity or extent of the genital tuberculosis and the viscosity of the semen

Turbidity was increased in the more extensive and active genital cases In these cases the specimens had a more yellow to yellowish-white appearance than normal and contained pus cells, immotile sperm, and cellular detritus

Morphology of the spermatozoa was not affected by the genital tuberculosis There was no increase in the number of abnormal forms and even in the presence of oligospermia, pus cells, and positive semen cultures for tubercle bacilli the differential counts of the stained smears were normal See figure 7

Motility of the sperm was below 60 per cent in 15 cases and below 80 per cent in another 5 cases In the 6 cases with motility above 80 per cent at 1 hour, one showed a drop of motility from 90 per cent in 1 hour to 10 per cent at 4 hours Specimens from patients with more active and extensive lesions contained many sluggish and immotile forms, many pus cells, and epithelial cells

Eleven patients had normal sperm counts per cubic centimeter but with volumes below one and two cubic centimeters All of these showed prostatic lesions and dilated prostatic ducts Four patients had normal analyses by both volume and count, but only one of these had normal initial motility (80–90 per cent), two had poor motility (20 per cent), one had decreased motility (60 per cent)

Although only one of the 53 patients studied by semen analysis could be considered to have a completely normal analysis, genital tuberculosis did not entirely preclude the possibility of a fairly good sperm *count* One married patient with advanced renal tuberculosis, bilateral epididymal nodules with calcification, thickened vasa, prostatic involvement, and dilated prostatic ducts, had a sperm count of 178 0 million per cubic centimeter, a 1 2 cc volume, and 80 per cent motility Another with bilateral renal tuberculosis, a soft prostate, dilated prostatic ducts, and a positive semen culture for tubercle bacilli, had a count of 157 0 million per cubic centimeter, 2 0 cc volume, and 90 per cent motility at 1 hour with a drop of 10 per cent motility at 4 hours

Histological study of the testes adjacent to epididymal abscesses showed no characteristic picture See figure 8

Spermatogenesis was present but depressed In one case with a long tuberculous history, there was considerable secondary tubular atrophy, but occasional primary spermatocytes were still noted The general debility and chronicity no doubt contributed to the testicular atrophy in this case The effect of genital

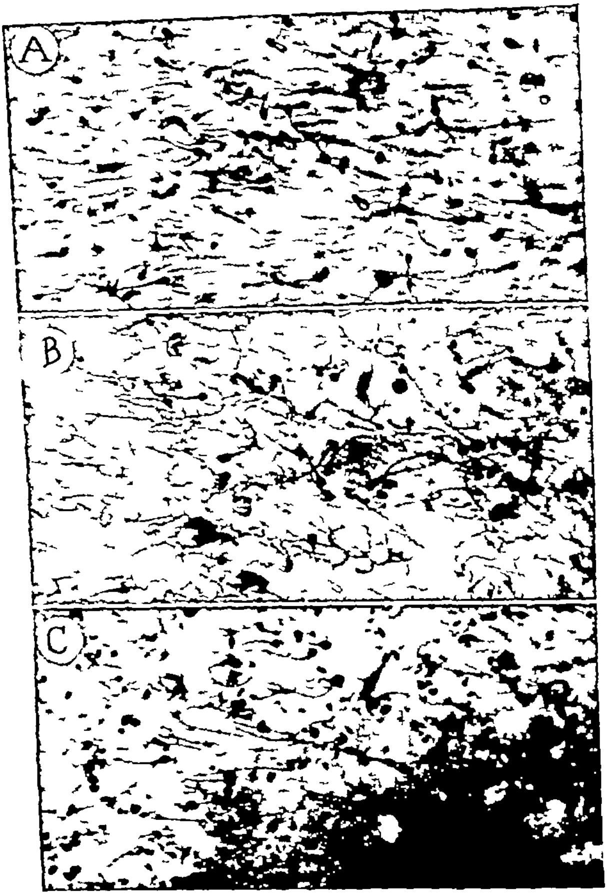


FIG 7 Samples of stained smears for morphology of spermatozoa from patients with genital tuberculosis Infection had no effect upon morphology of sperm Differential counts were within normal limits

tuberculosis on the testes was one of simple tubular blockage plus the secondary atrophy of debilitating disease This was supported by the frequent finding of clumps of normal spermatozoa in the blocked epididymal tubules of the excised epididymides (fig 9) and by the essentially normal morphology noted in semen analyses Low grade fever associated with the chronic disease may have also depressed spermatogenesis

The combination of decreased volume of ejaculate from the prostatic tuberculosis, blocked epididymal tubules and vasa from fibrosis and edema, and increased turbidity and decreased motility from the inflammatory process accounted for the abnormalities of the semen analyses in these cases of genital tuberculosis

Semen cultures for tubercle bacilli In only one case was a history obtained of vaginal discharge in the wife She was examined and no evidence of tuberculous cervicitis or vaginitis was found In one other patient, the positive semen had caused a tuberculous ulcer on the wife's posterior vaginal fourchette In view of

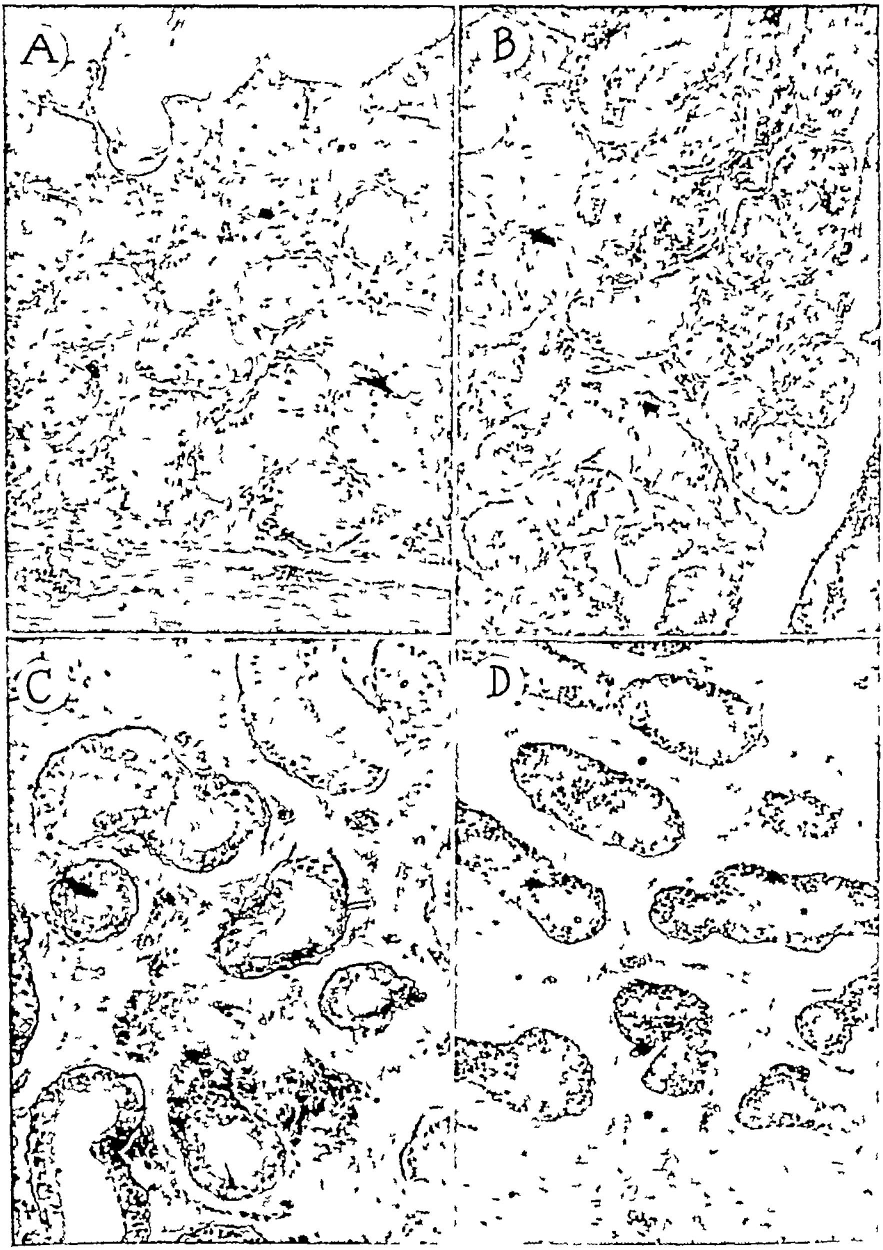


FIG 8 *A*, section of testis adjacent to tuberculous epididymal abscess Depressed spermatogenesis is present but spermatocytes and sperm can be seen in tubules *B*, biopsy of testis adjacent to larger tuberculous epididymal abscess is similar to *A* *C* and *D*, testicular tubules in patients with tuberculous epididymal abscesses show considerable secondary atrophy

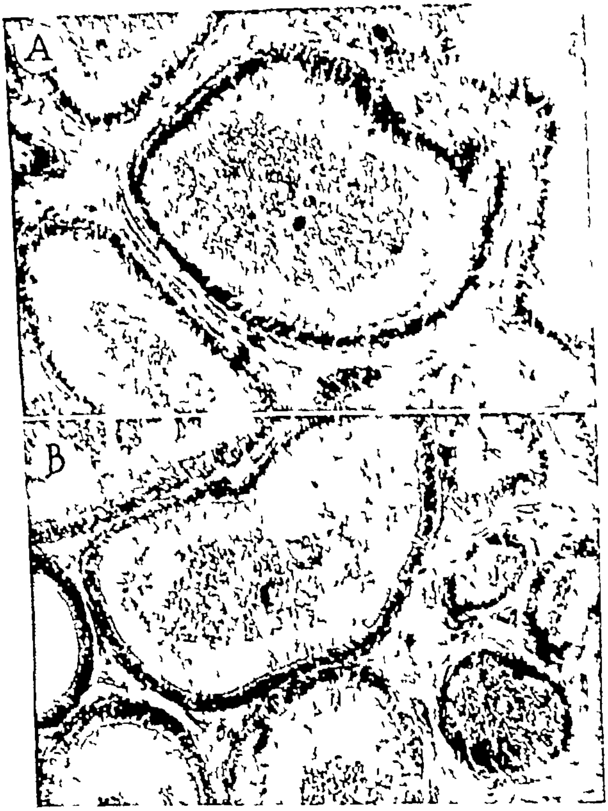


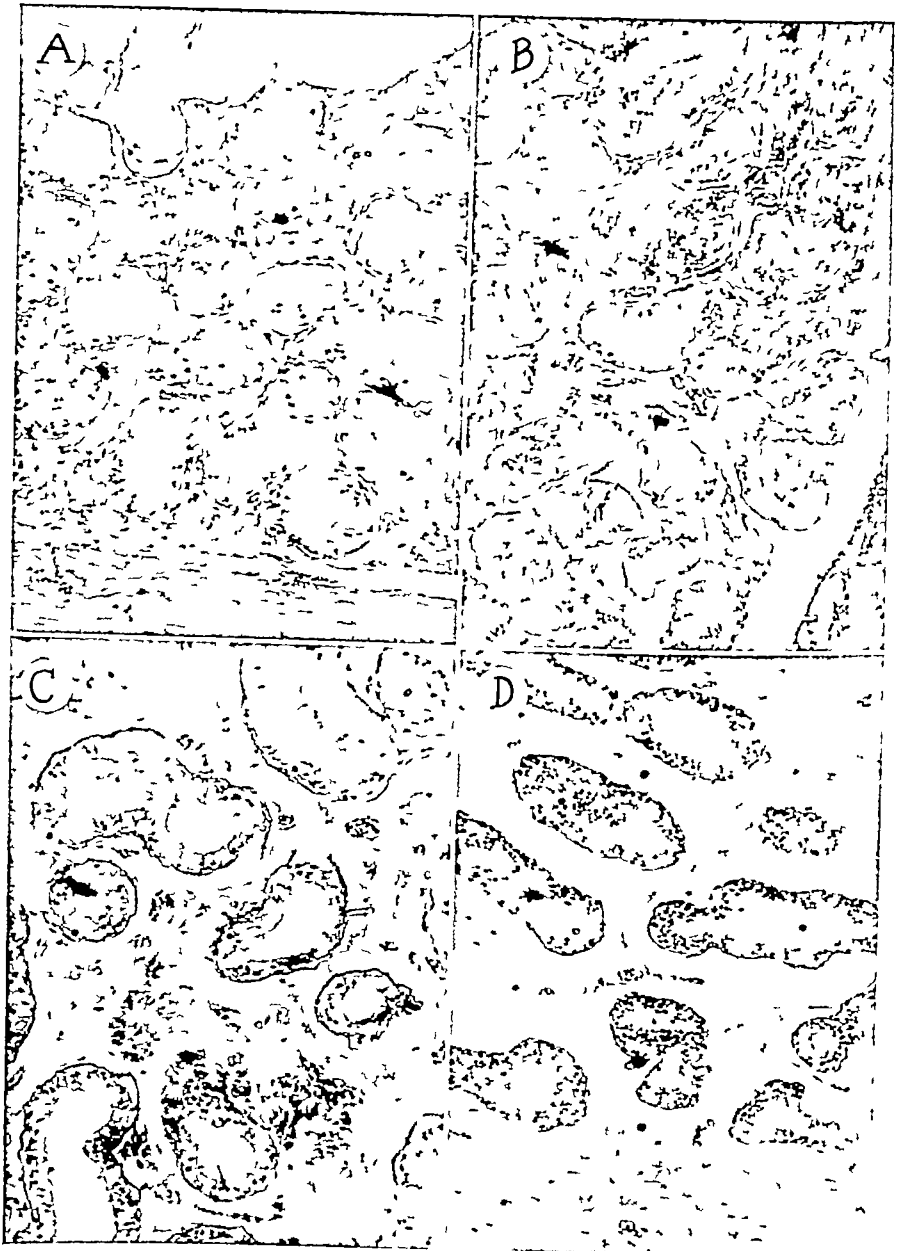
FIG 9 Sections show epididymal tubules filled with spermatozoa Spermatogenesis has persisted in testis even though occlusion in ductus deferens has blocked exit of sperm from epididymal tubules

the positive semen cultures obtained and the case of tuberculous vaginal ulcer reported by Lattimer, et al, all of the patients were advised to use a condom during intercourse, until the disease could be considered arrested

Semen cultures for tubercle bacilli were made in 35 cases Specimens with a volume of at least 2 0 cc were treated and digested with 23 per cent hydrated tri-sodium phosphate and incubated for a minimum of 15 hours The specimen was then centrifuged and the pH of the sediment adjusted to 6 7 using 1 N hydrochloric acid (digestion of the specimen lowered the incidence of contaminants) After further centrifugation the sediment was streaked on two slants of NTA medium and incubated at 37 degrees centigrade for six to eight weeks

Specimens with volumes below 2 0 cc were not treated in this manner but were merely taken up with a sterile swab and direct smear and culture made

Of the 35 patients with adequate volumes for smear and culture, four (11 per cent) were positive for tubercle bacilli on culture All four cases had prostatic involvement, dilated ducts were present in three and a trabeculated red posterior urethra in the other case A flocculent exudate protruded from the dilated ducts in one of these 4 patients



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abscessed epididymides or when the tuberculous epididymal focus is a constant source of urinary infection

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Three of the patients had volumes sufficient only for smears for acid-fast bacilli, and one of these was positive for tubercle bacilli He had prostatic involvement and golf hole prostatic ducts, left epididymectomy had been performed for tuberculosis At ejaculation he was able to produce only a few drops of a clear, colorless, thin fluid containing 0–1 white blood cell/high power field and no spermatozoa

TREATMENT OF GENITAL TUBERCULOSIS

The advent of chemotherapy has altered the management of genital lesions just as it has the management of renal lesions

At present, combined therapy with isoniazid, 100 mg t i d , and sodium PAS 5 gm t i d , given together for a period of 2 years, is advised for genital tuberculosis The plan is similar to that used routinely in renal tuberculosis Lower urinary tract symptoms are greatly relieved by the use of chemotherapy Radical prostatovesiculectomy is advised only in rare cases with intractable pain Epididymectomy is employed only for lesions which show intractable, secondary infection or sloughing, and the operation is followed by one year of combined chemotherapy

SUMMARY

The fertility and clinical pathology of sixty current patients with genital tuberculosis was reviewed at the Research Unit for Genito-Urinary Tuberculosis, Veterans Administration Hospital, Bronx, New York City Eighty-five per cent of the genital tuberculosis appeared to be secondary to renal tuberculosis Most of the epididymal tuberculosis was secondary to prostatic tuberculosis, although the ductus deferens was not thickened in 60 per cent of the cases

Fertility was found to be sharply reduced by genital tuberculosis Absent or scanty semen was an impressively frequent sequel to prostatic tuberculosis Total sperm counts and motility were usually reduced The presence of bilateral epididymal nodules did not block the vasa in all cases The morphology of the sperm was not affected and the testes showed only moderately depressed spermatogenesis The overall effect of genital tuberculosis on the testes appeared to be one of simple tubular blockage plus the secondary atrophy of debilitating disease

In 4 patients out of thirty-five, semen cultures were positive for tubercle bacilli, and in another a positive smear was obtained These findings demonstrate the possibility of transmission of the disease through the ejaculate This was borne out by one case of tuberculous ulceration of the wife's vagina

Since any chance of fertility is usually of great concern to the patient, it is now felt that all prostatic and epididymal tuberculosis should be treated by 2 years of chemotherapy, combining sodium PAS and isoniazid, and possibly streptomycin Epididymectomy is now advised only in the presence of acute abscessed epididymides or when the tuberculous epididymal focus is a constant source of urinary infection

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Since any chance of fertility is usually of great concern to the patient, it is now felt that all prostatic and epididymal tuberculosis should be treated by 2 years of chemotherapy, combining sodium PAS and isoniazid, and possibly streptomycin Epididymectomy is now advised only in the presence of acute with fibroplastic features such as interstitial cystitis, irradiation cystitis[6] and Peyronie's disease[7] Temporary favorable results have been reported in isolated instances of all of these conditions

TECHNIQUE

Adult male dogs, varying in size from 12–20 kg were used in this study Two series of four animals each served as the experimental and control groups respectively The same procedure was performed on each animal in both groups The control animals received no postoperative medication, while the experimental group received 50 mg of cortisone intramuscularly daily for 14 days

Under intravenous nembutal anesthesia and through a small scrotal incision, the vas deferens was exposed and transected at a level about 2 cm above the upper pole of the testes A 6–7 cm length of No 35 steel wire was introduced, as a splint, into the lumen of the proximal and distal ends of the vas and its distal end was brought out through a small puncture wound close to the tail of the epididymis An end-to-end anastomosis of the previously divided segment of vas was established, utilizing four No 5-0 arterial silk sutures These sutures were placed equidistally about the circumference of the line of approximation The distal free end of the splinting wire was anchored to the tunica albuginea by a single silk suture The scrotal wound was closed in layers using No 4-0 silk

Two weeks later the scrotum was opened again and the wire splint was removed Ten to twelve weeks after removal of the splint, bilateral orchiectomy and resection of the vas above the site of anastomosis were carried out At orchiectomy the patency of the fresh specimen of vas was determined by the injection of normal saline into the lumen of the vas through a No 24 or 26 needle The specimens were fixed in formalin for histological examination

The experimental animals received intramuscular cortisone, 50 mg daily, regardless of weight, after completing the initial operation, i e , the transection and reanastomosis This dose was maintained for 14 days postoperatively at which time the splint was removed The postoperative care of the animals differed in no respect other than the administration of cortisone in the experimental ones

DISCUSSION AND RESULTS

For this study vasovasostomy, rather than epididymovasostomy was chosen, because of the technical simplicity of this procedure, and because of the anatomically delicate structures of the experimental animals The wire splint was buried under the skin in order to prevent the animals from chewing or removing it The splint was sutured to the tunica albuginea in order to prevent it from working free, an accident which occurred in the first case

At the time of the removal of the splint, it was observed that the dissection

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[6] Persky L and Austen, G ACTH in radiation cystitis J Urol , 70 724–728, 1953

[7] Teasley, G H Peyronie's disease J Urol , 71 611–614, 1954

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THE EFFECT OF CORTISONE ON EXPERIMENTAL VASOVASOSTOM

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In a recent, detailed study of patients with complete asopermia upon whon exploration and corrective surgery were performed, it was reported that a successful surgical result, as indicated by the presence of sperm in the ejaculate was obtained in about 20 per cent of the cases Restoration of fertility wa achieved in no more than 8–10 per cent[1]

In another small series of vasovasostomies performed after preceding vasectomy, although the percentage of surgical success was appreciably greater, there was still a moderately high incidence of failure[2] Where failure occurred it was thought to be due probably to postoperative fibrosis and secondary obstruction

Because of the generally poor anatomic and physiologic results obtained after plastic surgery upon the vasa to restore continuity of the ducts, many technical variations have been devised in the technique of anastomosis in an effort to avoid postoperative strictures Since postoperative stenosis seems to be the principal complication of the successful restoration of ductal continuity, and since variations in the technique of anastomosis have not improved appreciably the overall clinical picture, it was believed that an experimental study should be undertaken to explore in this area the known inhibitory effect of cortisone on the fibroplastic reactions of tissues[3-5]

Several reports have been published recently presenting the favorable effects of the use of cortisone in the treatment of strictures[3, 4] Baker et al reported a series of urethral and ureteral strictures treated surgically with the concomitant administration of cortisone in 24 patients In 22 of these patients no further dilatation was required 6–9 months after cessation of cortisone administration

The same author[4] reported good results in cases of ureterointestinal anastomosis after the postoperative administration of cortisone He stated that cortisone has no effect on the healing of noninfected wounds, the increased fibroplastic reaction being reduced only in the presence of infection ACTH and cortisone have also been utilized in the treatment of other urological conditions

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Note by editor The senior author's briefcase containing the galley proof of this paper was stolen and only recently recovered The unfortunate occurrence is responsible for delay in publication of the paper

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with fibroplastic features, such as interstitial cystitis, irradiation cystitis[6] and Peyronie's disease[7] Temporary favorable results have been reported in isolated instances of all of these conditions

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TABLE 1

	Hematoxylin		Trichrome		Reticulum	
	Experim group	Control group	Experim group	Control group	Experim group	Control group
R	x	x	xxx	?	?	xx
L	x	x	?	xxx	xx	xxx
R	x	xxx	?	xxx	?	x
L	?	x	xxx	?	xxx	?
R	xxx	x	xx	x	x	?
L	xxx		x		x	
R	xxx	x	xxx	xxx	xx	x
L	x	xx	x	xxx	x	xxx

Degree of fibroplasia as estimated by 1 to 3 x The question mark means doubtful conclusions where no decision could be reached trying to classify the slide

in the experimental group was easier and that the scrotal layers were less adherent than in the control group

Ten to twelve weeks after the original operation, at the time of the orchiectomy and vasectomy, no significant differences in gross dissection and in patency were found between the two series Five of the eight experimental anastomoses were patent, while three of seven control anastomoses were patent One anastomosis in a control animal could not be tested because of separation of suture line during surgical removal of the specimen

All the specimens were submitted for histological examination Longitudinal sections through the anastomotic site were prepared and the slides were stained by three different methods (hexamethylene, eosin, thiochrome and reticulum stain)

The slides were studied without knowledge on the examiner's part of the group from which they were obtained The degree of fibroplasia in each instance was graded in a scale of 1 plus to 3 plus, and then the slides identified as to group Utilizing the different methods of staining, no significant differences in fibroplasia could be discerned between the two groups (table 1) A similar previous experimental study of the effect of cortisone on wound healing in dogs[8] revealed no difference in the rate and quality of healing in aseptic wounds

Although no definite benefit from the use of cortisone could be detected in our study, better results may be achieved with a modified technique, using a larger dose of cortisone, either systemically or locally To attain a high local concentration of the drug, a fine polyethylene tube could be used for splinting of the vas, preferably with perforations in the tube at the line of anastomosis [9]

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[8] Cole, J W , Orbison, J L , Holden, W D , Hancock, T J and Lindsay, J F A histological study of effect of cortisone on wounds healing per primam Surg , Gynec & Obst , 93 321–326 1951

[9] Hollander, J L , Brown, E M Jessor, R A and Brown, C Hydrocortisone and cortisone injected into arthritic joints J A M A , 147 1629, 1951

Another possible method of securing a more favorable result would be to start the administration of the drug several days prior to the initial surgery and to continue it for some time after removal of the splint, thereby hoping to extend the inhibitory effect of cortisone upon the fibroplastic reaction over a more prolonged period

However, before one attempts to apply the results of animal study to humans, it is well to reiterate that species differences are of great significance in any such experimental work, and in this instance at least the response of man to cortisone may be quite different from that of the dog

Further experimental studies along this line will be undertaken

SUMMARY

A series of dogs undergoing vasovasostomy has been studied to determine the inhibitory effect of cortisone on the local fibroplastic reaction No demonstrable inhibition was found

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HEMATOSPERMIA

MORLETON A MAGID AND JAMES H HEJTMANCIK

The observance of blood in the ejaculate has brought many patients to a doctor's office We have seen a number of patients with this complaint Review of the literature failed to reveal any significant amount of information on the subject Eisendrath and Rolnick,[1] discussing tuberculosis of the prostate and seminal vesicles state, "ejaculation is often painful and hemospermia can exist without seminal vesicle involvement " Hugh Young's[2] only comment on the subject is, "hematospermia may occur in prostatitis or tuberculosis and rarely in carcinoma or hypertrophy of the prostate Seminal vesiculitis is seldom noticed by patients " Herbst and Merricks'[3] review of seven hundred and thirty ejaculatory ducts that were catheterized because of seminal vesiculitis mentions hemospermia as one of the signs, assuming, we are certain, that the blood was due to mucosal ulceration The following study was stimulated by the findings obtained in studies of seminal vesicles of two patients who were seen because of hematospermia

CASE REPORTS

Case 1 A 52-year-old white man was first seen February 7, 1956 He stated that for the past month, upon ejaculation, he noticed that the ejaculate had been bloody This concerned him and he saw a doctor in his home town who felt that further investigation should be completed At first the ejaculate was purplish red in color and was obviously recent blood, however, more recently the ejaculate had been dark and chocolate in appearance The patient stated that intercourse had occurred approximately two times each week The patient further stated, upon questioning, that he had no pain or discomfort at any time, no suprapubic or perineal discomfort either upon ejaculation or at any other time A review of his past medical history failed to reveal venereal or tuberculous infections Upon rectal examination, the prostate was normal in size More firmness seemed to be present at its superior borders near the median sulcus but no nodules were present The prostate was smooth, firm, round, regular and freely movable Neither seminal vesicle could be palpated The voided urine was negative and no residual urine was present

The patient was admitted to Providence Hospital where, on February 9, 1956, under light pentothal anesthesia, cystoscopy, urethroscopy and seminal vesiculography were completed At cystoscopy, it was noted the bladder was normal in appearance Both ureteral orifices were present in the proximal corners of the trigone A urine culture obtained from the bladder was later proven negative The instrument was withdrawn into the prostatic urethra and a small, fibrous

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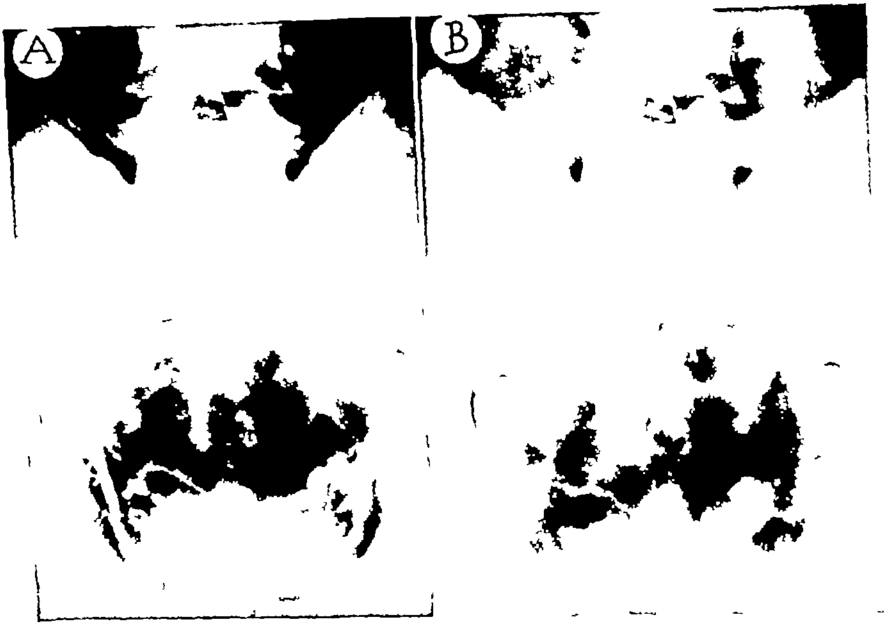

FIG 1 Case 1 A, seminal vesiculograms indicate chronic infection with dilatation of tubules Both external iliac veins are visualized *B*, films taken 30 seconds later show lack of medium within vascular system

median bar was noted No dilated mucosal blood vessels were seen in the region of the internal os The verumontanum was normal in appearance The utricle was catheterized and identified Then, each of the ejaculatory ducts was catheterized and catheters were passed 3 cm bilaterally Seven cubic centimeters of 50 per cent urokon were injected through the catheters and films made (fig 1) By accident, the first film was made before the total amount of opaque medium had been injected A delayed film was then made because of what appeared to be two extra duct systems on the lateral sides of the seminal vesicles The patient was returned to the x-ray department in order that intravenous pyelograms could help ascertain the location of the ureters Films of the pelvis, following injection of the opaque medium into the seminal vesicles, showed the structures well outlined The right vas deferens was shown Shadows were then seen on each side of the pelvis These appeared to be pelvic veins and were outlined by the injected contrast material Apparently, some close connection existed between the seminal vesicles and the pelvic venous system Following intravenous administration of the contrast material, prompt excretion occurred from both kidneys, as seen on the 5-minute film The pelves and calyces of the kidneys were satisfactorily outlined and appeared normal The ureters were in their usual positions and were medial to the previously seen venograms Following this procedure, the patient, while still in the hospital, experienced fever and pyuria which were treated with thiosulfil

Over the next 2 months the patient's mild prostatitis was treated by prostatic massage A number of condom specimens were brought to the office in order that we could do microscopic examinations of the specimens for blood None was found The patient was followed from February 1956, through May 1956, he had had no recurrence of hematospermia and the prostate had not changed in size, however, the prostatic secretion showed a marked reduction in the number of pus cells

Case 2 F R, a white man aged 47, was first seen February 20, 1956, at which time he gave the history that for the past year he had been having hematospermia At first, this was intermittent but for the past two or three months, the patient stated that all of the ejaculate was bloody and more recently, the blood had been brighter red rather than chocolate brown He had never had any blood in the urine The patient stated that of late he had a dull ache (rather than a severe pain) in the perineum and low in the right lower quadrant The patient stated that upon ejaculation he had some discomfort in the right lower quadrant, but not severe enough to prevent the act A specimen of urine failed to reveal any blood or pus cells The patient denied any history of past venereal or tuberculous infections The abdomen was negative on palpation and no pain could be elicited in the suprapubic area or right lower quadrant The external genitalia were those of a normal man No hernia was present The prostate on palpation was smooth, firm, round, regular and freely movable Above the prostate both of the seminal vesicles felt slightly distended and almost cystic Definite convolutions of the seminal vesicles were palpable because the patient was small in size and thin and this made readily accessible and palpable seminal vesicles It was believed that a small cyst of the right seminal vesicle was present because of the marble-like definitive feel of the lower pole of the vesicle The patient was requested to enter the hospital for cystoscopy and retrograde catheterization of the ejaculatory ducts for seminal vesiculography

On February 22, 1956, under light general anesthesia, a Lowsley-Peterson cysto-urethroscope was introduced Inspection revealed a normal bladder No

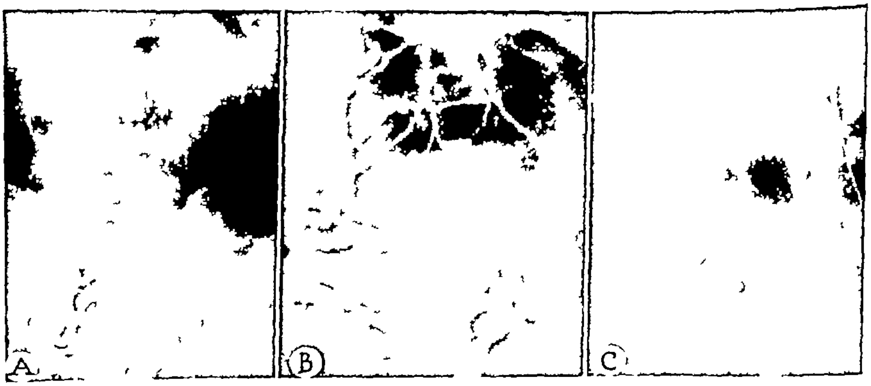

FIG 2 Case 2 *A*, *bilateral seminal vesiculograms visualize both ampullae and vasa* Demonstration of seminal vesicle venous communication on right side with filling of right internal iliac vein and its tributaries including junction with external iliac vein Vena cava is delineated as high as region of portal vein *B*, close up view of seminal vesicle vascular communication *C*, delayed film of same area reveals empty vascular tree

stones, tumor or prostatic enlargement were detected Inspection of the prostatic urethra revealed the verumontanum to be normal in appearance No dilated prostatic ducts were present Each of the ejaculatory ducts was present as was the utriculus masculinus Each duct was catheterized and following this, several vesiculograms were made by means of injecting and taking x-rays during the process of injection The plain urogram was negative for vesical and prostatic calculi Several small lateral phleboliths were present Films following injection of urokon into the ejaculatory ducts, showed the seminal vesicles quite well filled and essentially normal The vas was also filled down to the scrotum on both sides without apparent abnormality Of considerable interest was the fact that a large amount of dye was noted passing into the vascular plexus about the right vesicle and from this was filling the pelvic veins and the inferior vena cava practically to the liver A very small amount of dye was seen extending into one vein about the left vesicle The plexus about the right vesicle showed apparently a little dilatation of several of the vessels and a little irregularity of the lumen suggesting a mild varicose condition See figure 2

Following discharge of the patient from the hospital, the urine was found to have about twenty-five pus cells per high power field Achromycin was prescribed even though he was feeling fine

When seen in the office March 6, 1956, he stated that the ejaculate was now chocolate brown in color The urine at this time was negative The prostate and seminal vesicles were palpated and found to be distended The prostatic cell count revealed a packed field of pus The prostate seemed to be more boggy than previously noted and over the next 5 months regular prostatic massage was instituted The hematospermia immediately cleared The patient received adequate therapy for the prostatitis and the hematospermia ceased only to recur on September 10, 1956 At that time the prostatic and seminal fluid was again packed with red blood cells The patient had moderately severe discomfort in the right lower quadrant that was believed to be due to infection of the seminal vesicles which caused seminal colic The prostatitis was treated regularly and on September 29, 1956, the patient again noticed that his semen contained blood The urine was negative The prostate was small in size and the prostatic fluid contained about two hundred pus cells per high power field and many red blood cells On October 2, 1956, the patient again experienced some right lower quadrant abdominal discomfort and noted that every time he voided, quite a bit of blood preceded the urine which would finally become clear A slight amount of penile discomfort was present The right seminal vesicle was palpated along with the prostate and no mass, fixation or tenderness was noted Because of lack of tenderness of the seminal vesicle at this time, it was believed that the patient should return for cysto-urethroscopy, to be certain that a tumor of the urethra was not present When seen October 10, 1956, the patient was comfortable and he had no pain in the right lower quadrant No blood was noted in the semen and there was none in the urine Microscopically, the urine was negative and all medication was discontinued

DISCUSSION

The accidental making of the x-rays while injecting the medium rather than at the termination, led us to the finding of the seminal vesicle-venous communication Braasch and Emmett,[4] in describing the technique after catheterization of the ejaculatory ducts injected, slowly, approximately two cubic centimeters of 35 per cent–50 per cent neoiopax or skiodan Films were then exposed immediately after injection was completed We have been able to reproduce our findings of the seminal vesicle-venous communication in several patients with hematospermia On several occasions when performing cystoscopy for reasons other than hematospermia, we catheterized the ejaculatory ducts and distended the seminal vesicles In no instance were we able to demonstrate venous filling in this group

The Lowsley-Peterson cystoscope was used exclusively The procedure was done under light pentothal anesthesia although we have proceeded to completion without any anesthesia or analgesia Preliminary shrinking of the edematous or granular posterior urethral mucosa, as suggested by Merricks, and Peterson and Luys, was not done The need for anesthesia is primarily due to position of the cystoscope sheath when in the prostatic urethra, being at approximately an eighty degree angle with the urethra in order to have a direct "shot" with the catheters into the ejaculatory ducts As suggested by Braasch and Emmett, small amounts of radiopaque medium were used at first Sodium iodide, 50 per cent, approximately two to three cubic centimeters, was used With the advent of 70 per cent urokon and miokon, these materials have been used in concentrated form in order that better delineation of the organs could be obtained The Lowsley-Peterson instrument has been preferred because the working elements are left in place and the telescope can be retracted so that a third dimensional view of the area is obtained and the procedure is simplified While an assistant is injecting the catheters which have been passed from one-half to three centimeters down the ejaculatory ducts, visualization of the verumontanum is maintained If there is no reflux of the injected medium issuing around the catheters between it and the ejaculatory ducts, from three to five cubic centimeters of 70 per cent opaque medium are injected However, in almost all instances, reflux is present, more injection pressure is exerted and a film is exposed When eight of the ten cubic centimeters have been injected into each catheter this film is taken much as the first films in translumbar aortography The cystoscope and catheters are maintained in position while the x-ray films are developed in order to be able to repeat the procedure or change the catheter position in the event that visualization of one of the seminal vesicles is unsatisfactory

In order to better understand the presence of blood in the seminal vesicles, their arterial and venous supplies must be reviewed The greater part of the arterial supply of the seminal vesicles is from the superior vesical artery which is a small branch of the hypogastric artery The superior vesical artery supplies the bladder but gives off the middle vesical artery which supplies the base of the bladder, prostate and seminal vesicles The inferior vesical artery usually arises in common with the middle hemorrhoidal artery and supplies the fundus of the bladder prostate and seminal vesicles. Of more importance in the present discussion is venous drainage of the seminal vesicle. The prostatic veins form a well marked prostatic plexus which lies partly in the fascial sheath of the prostate and communicates with the pudendal and vesicular plexuses. The venous plexus envelopes the lower part of the bladder and base of the prostate and communicates with the pudendal and prostatic plexuses drained by the vesicle veins into the hypogastric veins. The hemorrhoidal plexus consisting of an internal and external group of veins surrounds the rectum and communicates in front with the vesical plexus. The lower part of the external plexus is drained by the inferior hemorrhoidal veins with the internal pudendal vein. The middle part is drained by the middle hemorrhoidal vein which joins the hypogastric vein and the upper part joins the hypogastric and also forms the beginning of the inferior mesenteric vein which is a tributary of the portal system. A free communication between the portal and the systemic venous systems is established through the hemorrhoidal plexuses. Not described but beautifully illustrated in the plates of Gray's Anatomy[5] is a large and direct communicating vein between the internal and external iliac veins. The presence of such a vein makes the explanation of the x-rays obtained in case 1 possible, as will be shown later.

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[4] Braasch W F and Emmett, J L Clinical Urography Philadelphia W B Saunders Co 1951 p 608

Seminal vesiculography has never achieved widespread use as a diagnostic procedure due to the difficulty in catheterizing the ejaculatory ducts perforation and extravasation of the opaque medium. Of recent times, there is not the need to dilate the ejaculatory ducts as there seemed to be in the days prior to the sulfonamides and antibiotics when gonorrhea was more prevalent and the treatment prolonged. According to prior authors (Luys Merricks Rolnick, Peterson[6]) strictures of ejaculatory ducts developed on apparently the same basis as strictures of the urethra.

A review of the x-rays of case 1 suggests to the authors that duct communications existed between minor branches of the external iliac veins bilaterally and that upon filling the seminal vesicles with the radiopaque medium, both of the external iliac veins are filled up to their junction with the internal iliac veins. This finding is bizarre because the major venous return from the seminal vesicles is supposedly into the middle and inferior vesical plexuses which then communicates with the internal iliac veins.

In case 2, the x-rays very clearly show that there is a direct communication between vessels of the middle and inferior vesical plexuses and the internal iliac vein on the right. Interestingly enough, the radiopaque medium outlines the junction of the internal and external iliac veins and numerous small branches of the internal iliac and common iliac veins. The vena cava is outlined as high as the diaphragm. The exact mechanism of the communication between the lumen of the seminal vesicles and blood vessel is not understood. This probably exists as a thinning of the seminal vesicle walls, probably due to ulceration with direct erosion into the thin walled veins. In both cases presented the patients had chronic prostatitis, and radiologically the seminal vesiculograms nicely fit the classification of chronic catarrhal seminal vesiculitis by Peterson In case 2, the seminal vesicle only was involved

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[5] Gray's Anatomy of the Human Body, 21st ed. Philadelphia: Lea & Febiger.

[6] Peterson, A. P.: Retrograde catheterization in diagnosis and treatment of seminal vesiculitis. J. Urol., 39: 662–667, 1938.

In both patients the hematospermia became quiescent with antibacterial therapy and treatment of the prostatitis and seminal vesiculitis by rectal massage A final consideration at this moment concerns the occasional septic febrile reaction that occurs after manipulation per urethram Occasionally, due to thinness of the seminal vesicle walls, bacteria can readily be disseminated into the vascular system causing fever and chills It is possible that a similar mechanism exists in the septic reaction that sometimes follows simple cystoscopy and involves the bladder and urethral walls

CONCLUSIONS

Direct communication between the venous system and the seminal vesicle lumen is offered as a cause for hematospermia

A technique for the demonstration of both the seminal vesicles and communicating veins is offered

A direct avenue for bloodstream infection is suggested in the light of the seminal vesicle venous communication

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ANOTHER SELF-MANAGED BLADDER TRAINING DEVICE FOR TETRAPLEGICS

A ESTIN COMARR

From the Paraplegia Service, Veterans Administration Hospital, Long Beach Calif and the Department of Urology School of Medicine, College of Medical Evangelists, Los Angeles, Calif

A satisfactory self-managed bladder training device for tetraplegics was recently described by this writer

The purpose of this communication is to present a still more practical device which is not space-consuming and can be used either in bed or in a wheel-chair

The device is a remotely operated shut-off clamp which is normally closed, thus compressing the tubing leading from the bladder By bringing the jaws of the activating handle together, the compression on the tubing is released and the bladder is emptied The handle requires a minimal amount of pressure and

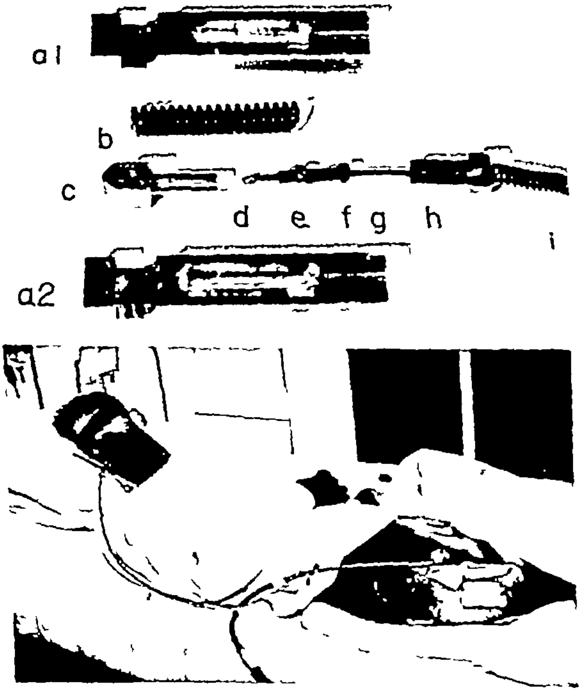

FIG 1 Device A (Upper), integral parts are *a 1* and *a 2*, two halves of mechanical box or body *b* Compression spring *c*, Plunger *d*, Spring wire *e*, Adjustable nut *f*, Adjustable screw *g*, Continuation of spring wire through spring housing *h*, Adjustable housing nut *i*, Spring housing

(Lower), patient biting down on activating handle of device A Note that rubber tubing goes through mechanical box at right angles

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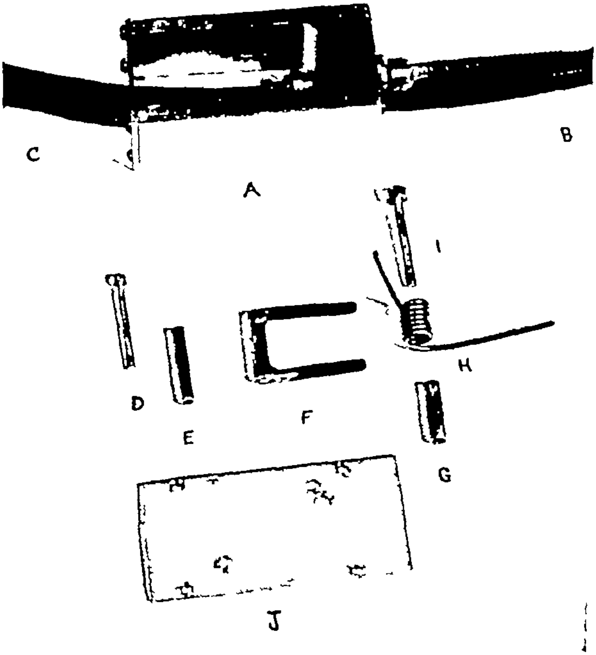

Fig 2 Device B Integral parts are *A*, mechanical box or body *B*, flexible spring housing *C*, rubber tubing *D*, guide pin *E*, roller for guide pin *F*, compression arm *G*, bushing for inside spring *H*, compression spring *I*, pin for holding spring and roller *J*, cover

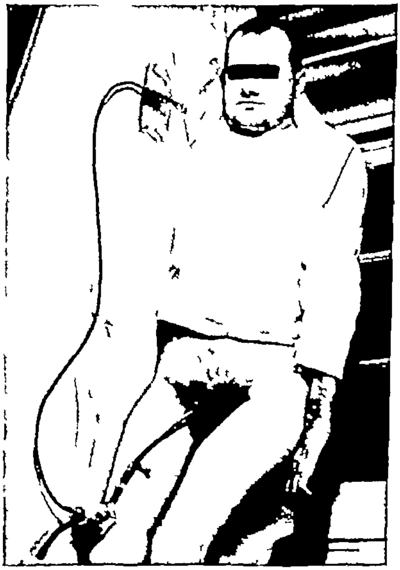

Fig 3 Activating handle placed in such a manner that pressure can be exerted on it by forearm or hand by tetraplegic patient who has voluntary motion in shoulders Note that device B is used and that rubber tubing goes through long axis of mechanical box

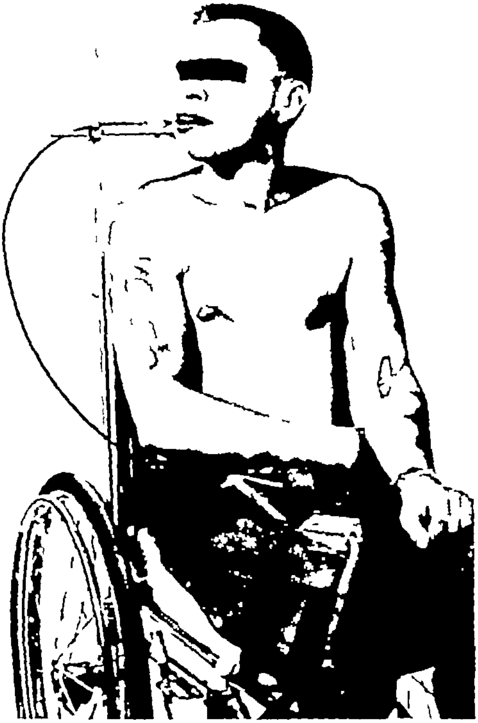

Fig 4 Tetraplegic patient without voluntary motion in both upper extremities Activating handle is adjusted to proper position for patient to grab with mouth Note that device B mechanical box is used for wheel chair

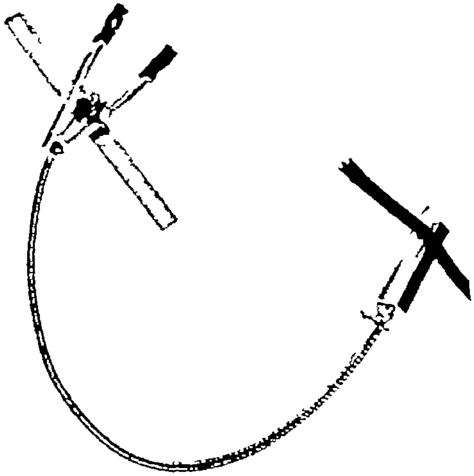

Fig 5 Activating handle is shown to bring out more detail Handle is used with both mechanical boxes In photograph, device A body is attached

therefore can be easily activated by pressure of the teeth in tetraplegics who have no voluntary shoulder movement For those quadriplegics who have voluntary shoulder control, the pressure of the forearm when applied on the handle is sufficient to activate the device

Two types of mechanical boxes can be used Device A (fig 1) is very satisfactory for bed use It is slightly awkward for wheel-chair use since the rubber tubing goes through the mechanical box at right angles Device B (figs 2, 3 and 4) is satisfactory for both bed and wheel-chair use since the tubing goes through the long axis of the mechanical box

SUMMARY

A very practical self-managed bladder training device for tetraplegics is described Two types of mechanical boxes are presented

The author wishes to acknowledge his appreciation to Mr John Demer, Investigative Medicine Section, for machining the parts and to the Medical Illustration Department of the Veterans Administration Hospital, Long Beach, Calif

REFERENCE

COMARR, A E A self-managed bladder training device for tetraplegics J Urol , 76 200, 1956

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THIXOKON AN IMPROVED URETHROGRAPHIC MEDIUM

JOHN DENMAN

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From its incipiency in 1910, there has been a basic dissatisfaction with urethrographic media The problem is that an oily medium sometimes forms emboli in the vascular system whereas an aqueous medium, although safe, is of too low a viscosity to produce satisfactory filling of the urethra

That an oily medium is responsible for immediate death, is well documented by autopsies done following urethrograms and hysterosalpingograms using oily contrast media Grossman reported 15 cases that he had found in the literature Also, cases have been recorded of death following injection of oil into the urethra for the purpose of dilating difficult strictures

Cunningham was the first to introduce the urethrogram when he described the technique in 1910 As a matter of historical interest, a reproduction of one of his published urethrograms is included (fig 1) He used 1 or 2 drams of a 50 per cent solution of argyrol injected with a syringe and held in the urethra by his clamp The subject was placed in the sitting position so as to present the thinnest portion of the body to the x-ray beam Later, to better orient the rather indistinct picture, he used a penny placed in the rectum at the apex of the prostate

Lipiodol was first used in 1922 by Sicard and Forestier and has proven to be a popular medium till of late However the basic difficulty persisted, namely, the danger of death from emboli Carr and Johnson, after summarizing the literature, concluded that the amount of intravenous oil necessary for death was highly variable, that the danger of embolism is greatly increased after previous urethral instrumentation, and that as a result nothing should be injected into the urethra that could not be safely injected intravenously

The problem then is twofold that urethrographic fluid must be safe if it enters the vascular system and that the solution must be viscous enough to distend the urethra and remain in position long enough to secure a good film The Mallinckrodt Chemical Works of St Louis has developed a new medium that appears to satisfy these requirements It is called thixokon and consists of two components a viscous aqueous vehicle combined with the regular 50 per cent urokon dye used in excretory urograms The viscous base is aqueous and therefore is felt to be safer in the event it should enter the vascular system It has been experimentally injected intravenously into animals without ill effect In addition, it has the useful property of thixotropy This is defined as the property of a solution which causes an increased viscosity when the solution is at rest Practically, this means that the solution may be injected with comparative ease but once injected its viscosity will increase and it will tend to be retained in the organ to be visualized

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Note by editor The galley proof mailed in the fall of 1956, failed to reach author due to a change of address Corrected proof not received until May 6, 1957

Present address 3707 Gaston Dallas, Texas

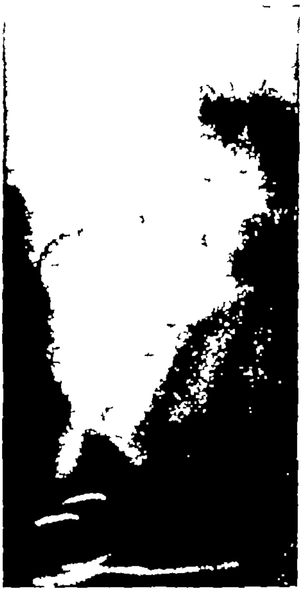

Fig 1 Early urethrogram, 1910

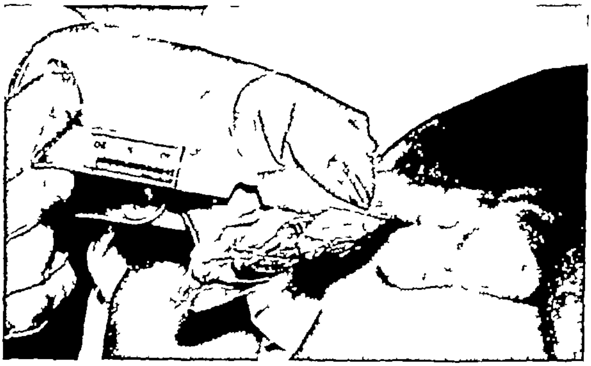

Fig 2 Technique of injection

The technique of injection as shown by the picture has not varied (fig 2) A 20 cc plain tip syringe with 20 or 30 cc dye is used A 10 cm portion of a 14F rubber catheter is fitted on the end of the syringe and leaded gloves and apron protect the operator The patient is placed in the right oblique position with his ankles crossed and with the central ray of the tube directed just below the symphysis pubis The catheter is inserted part way into the urethra and with the operator's left hand firmly grasping the penis and catheter, the injection is slowly begun A period of about 20 seconds is used for the injection

This new medium has been used in 110 cases with great satisfaction In none of these cases was there a death or an allergic reaction The patients were men varying in age from 14 to 87 years The urological problem was usually urethral stricture or prostatism A code system of rating was employed grade 1, excellent quality, grade 2, satisfactory, grade 3, poor, grade 4, unsatisfactory The result of the survey is as follows grade 1 comprised 80 cases, grade 2 comprised 28 cases, grade 3 comprised 2 cases, and grade 4 comprised none of the cases

Several x-rays of urethral strictures are presented as examples of good opacity combined with sufficient viscosity to adequately fill the urethra (fig 3)

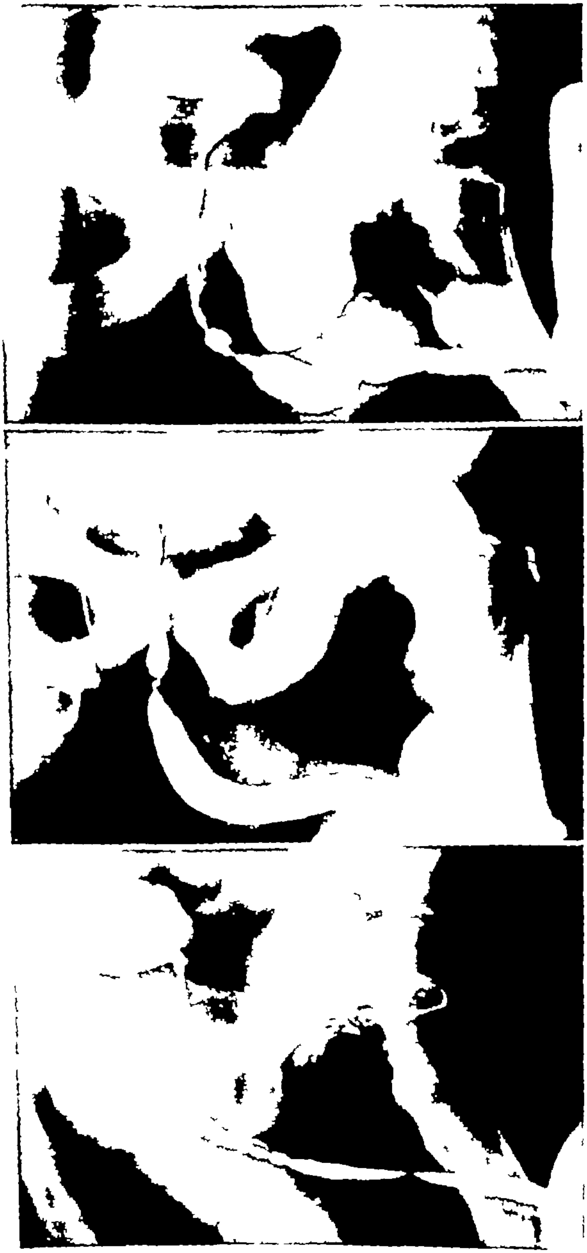

FIG 3 Urethrograms made with thixokon

SUMMARY

Thixokon, a new urethrographic medium, has proven quite satisfactory in 110 cases It employs a new viscous vehicle which has two advantages an aqueous body and a thixotrophic property Urokon is used as an admixture for radiopacity

Acknowledgement is made to the Mallinckrodt Chemical Works for liberal supplies of thixokon and also to Williams and Wilkins Company for permission to reproduce the early urethrogram

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A NEW RECORDING UROFLOMETER: A SIMPLE AUTOMATIC DEVICE FOR MEASURING VOIDING VELOCITY

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Because of ingenious implements and tests, relatively little guess-work occurs in urological diagnosis. In addition, new improvements are constantly being added to make the field of urology more accurate and objective. Tests of the functional aspects of micturition have lagged in this respect perhaps, and to some extent we have relied on subjective findings and interpretations. Several methods have been described to add objectivity to this problem. In 1932, Ballenger suggested measuring the distance a man could project his stream as an aid in measuring the degree of prostatic obstruction.[1] In 1940, Sigematu briefly described a "slit-flow-clock apparatus" for measuring urinary flow, but apparently could not foresee its practical application.[2] In 1948 and 1954, Drake described two different types of uroflometers which he believed were of value in assessing urinary flow in normal persons and in patients with obstructive voiding problems.[3, 4]

For the last 5 years we have been using a uroflometer which has been helpful in determining the degree of functional impairment caused by various obstructive and neurogenic lower urinary tract lesions. It also has been useful in evaluating the results of treatment in these conditions.

The present model of our instrument was conceived by Dr. David H. Kuntz, improved by Dr. Stanley Moulton and the author, and perfected and produced by the Charles Meriam Company.* The prototype upon which the mechanics of this uroflometer are based was described by Drake.[3] Drake's original uroflometer operated on the principle of recording increasing weight of urine passed against a time factor. Although the apparatus which he described appeared to be fairly accurate for volumes of urine over 150 ml., its construction was rather crude and cumbersome and it was not produced commercially.†

Accepted for publication February 28, 1957.

[1] Ballenger, E. G., Elder, O. F. and McDonald, H. P.: Voiding distance decrease as important early symptom of prostatic obstruction. South. Med. J., 25: 863, 1932.

[2] Sigematu, S.: Uber das Urinogram. Hihu to Hitunyo, 8: 42, 1940.

[3] Drake, W. M., Jr.: The uroflometer: An aid to the study of the lower urinary tract. J. Urol., 59: 650, 1948.

[4] Drake, W. M., Jr.: The uroflometer in the study of bladder neck obstructions. J. A. M. A., 156: 1079, 1954.

* Charles Meriam Co., Los Angeles, Calif., manfacturer. Distributed by V. Mueller & Co., 330 S. Honore St., Chicago 12, Ill.

† Because of the complicated apparatus and calculations required to obtain maximum flow rates, Drake believed that his original device was not suited for general office use. He subsequently described a simplified apparatus based on the principle of serial filling of multiple chambers through graded overflow vents in a weir type of receptacle.[4] This apparatus has the advantage of being simple, accurate and of professional appearance, but is not an automatic recording device and, therefore, no permanent record of the type of voiding in a given individual is obtained.

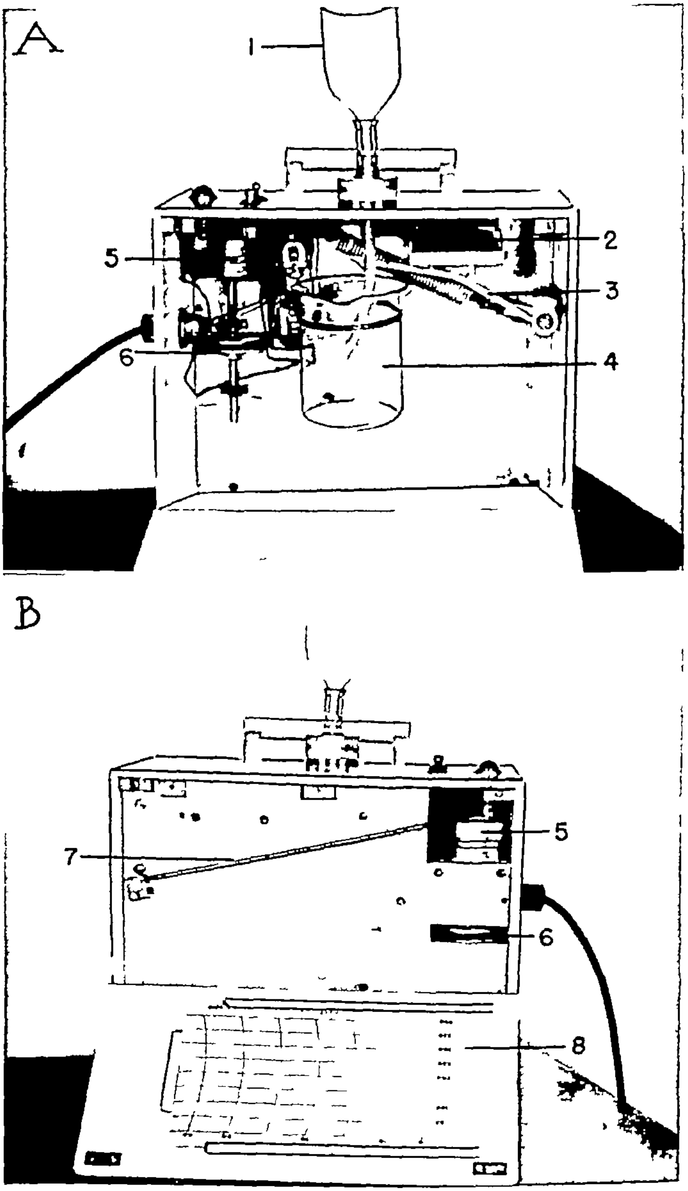

FIG 1 *A*, back view of uroflometer *1*, Voiding funnel, *2*, dry cell battery, *3*, lever arm, *4*, urine metering cup, *5* motor, *6*, rubber wheel chart drive

B, front view of uroflometer *5*, Motor, *6*, rubber wheel chart drive, *7*, recording arm, *8*, chart—uroflogram

We believe that we have achieved certain advantages in our uroflometer which makes it practical for routine office use The apparatus is housed in a small, compact, single unit which is neat, attractive and portable The complete unit measures 12 by 10 by 7 inches and weighs 10 pounds A small electric motor drives a rubber wheel which propels the recording chart at a constant rate

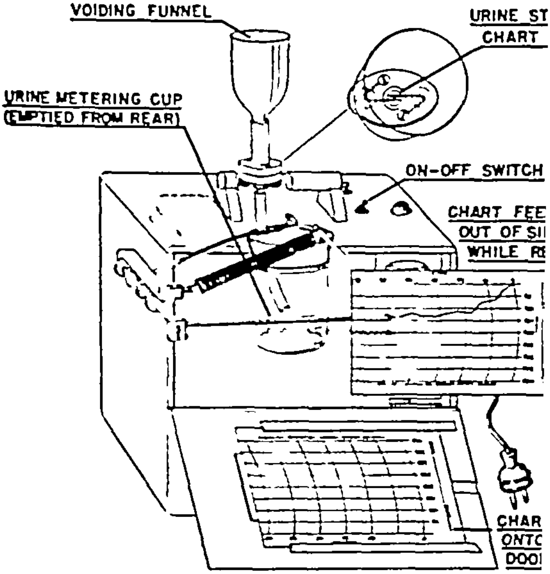

FIG 2 Schematic (composite) drawing to show operation

through a slot in the rear of the housing The patient vo (washable) funnel which directs urine flow into a beaker s The weight of the voided urine in the beaker is transmitte a recording stylus which inscribes a path on the chart as i and 2) The charts are printed with ordinates representin tervals and with abscissae representing 50 ml volume in urine converted to volume on the card) A solid stylus, in wheel to minimize friction, records on a wax coated card, for ink

The motor in our uroflometer automatically drives the c trolytes) passing through the inflow tube contacts electrode trical circuit This allows the patient to have privacy durin micturition, thereby adding to the reliability of the test W degree of hesitancy is desired, the patient can start the separate switch and the time lapse prior to the initiation can be recorded

Figure 3 depicts voiding curves in a normal male and

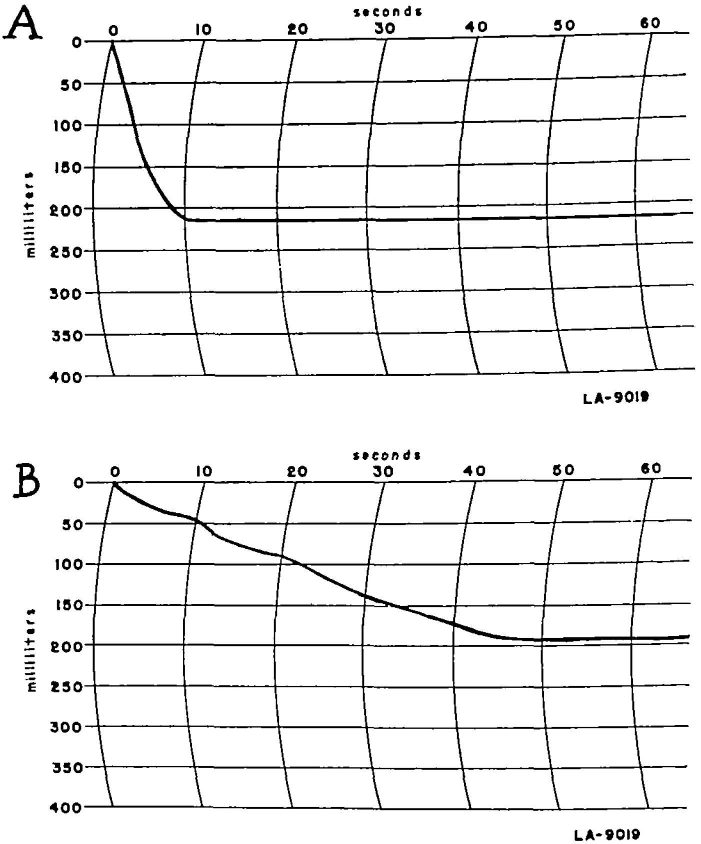

Fig 3 *A*, normal uroflogram Maximum voiding rate, 26 6 cc per second *B*, uroflogram illustrating impaired voiding velocity in patient with obstructive prostatic enlargement Maximum voiding rate, 6 7 cc per second

We have had extensive clinical experience with this uroflometer and have made over 2000 recordings on normal patients and patients with various types of voiding problems We have found that a minimum voided volume of 150 ml is necessary for an accurate determination of the urine velocity, that normal range of maximum urine flow is from 20 to 44 ml per second in both male and female adult patients, that the normal range of maximum urine flow is from 13 to 26 ml per second in children between the ages of 4 and 13, that in both normal and impaired micturition, the maximum voiding velocity is constant or nearly so on repeated testings, provided the urine volume is over 150 ml

INDICATIONS

1) *Obstructive prostatic enlargement* In these cases, the velocity of urine flow is usually altered before bladder decompensation occurs Therefore, estimation of the urinary stream is important in the early evaluation of the problem Because of the insidious nature of the disease, the patient may be unaware of the degree of impairment of his voiding velocity and frequently there is disparity

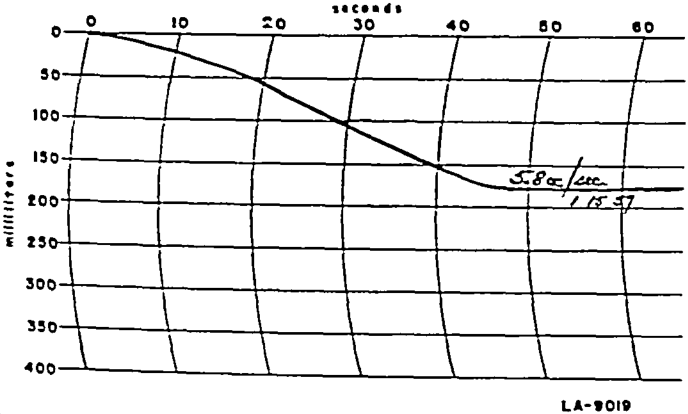

FIG 4 Uroflogram of patient with persistent urinary symptoms but without residual bladder urine 5 months after transurethral prostatectomy It shows impaired micturition and suggests incomplete resection Residual prostatic tissue was found on cystoscopy

between the type of urination he describes and the type of urination he actually has Prather[5] in discussing indications for elective prostatectomy has this to say, "Prostatectomy is unlikely to improve the symptoms of frequency urgency and nocturia in a patient without a bladder residual of 60 cc or more, but will improve a slow or thin hesitant urinary stream Thus prostatectomy may at times be indicated in the man with a residual of less than 60 cc The term 'slow stream' is a relative one which should be witnessed by the experienced eye of the urologist rather than accepted sight unseen " Since the automatic uroflometer provides an accurate record of the patient's voiding pattern it eliminates the subjective interpretation of both patient and urologist In patients with borderline bladder residuals, the uroflogram (performed on two or three occasions) may be a reliable method of determining the need for prostatectomy

Postoperatively, the uroflometer provides for the patient as well as the urologist objective evidence of the degree of benefit achieved Similarly, it can be used as a guide for the necessity for postoperative urethral dilatation and as an indication of incomplete resection or bladder atony in the patient with persistent problems of micturition following surgery (fig 4) We have also employed the uroflometer to aid in determining the degree of benefit achieved in treating patients with prostatic enlargements by nonsurgical means[6]

2) *Urethral stricture* The uroflometer has proven of inestimable value in determining the degree of obstruction in problems of urethral stricture Frequently in these cases, there is no significant residual bladder urine even with extreme slowing of the urinary stream Post-dilatation uroflograms attest to the efficacy of treatment and are helpful in determining the proper interval between urethral dilatations

Urethral and urethrovesical strictures in woman comprise a large portion of the urologist's practice Symptoms are often vague and descriptions of the type of micturition are frequently unobtainable Standard urological examinations are many times unrevealing and empirical trials of urethral dilatations are given The uroflometer serves a useful purpose in evaluating the degree of obstruction and in determining the need for dilatation or bladder neck surgery in these patients No problems have been encountered in having women use the uroflometer They are instructed to sit on the edge of a chair, place the funnel under the perineum and void naturally The patient can easily grasp the significance of the problem when the uroflogram is explained to her Frequency of treatments can be determined by the uroflogram on repeated performances

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[5] Prather, G C Elective prostatectomy J Urol 76 131 1956

[6] Kaufman J J and Goodwin, W E The effect of combined androgen-estrogen therapy on benign prostatic hypertrophy To be published

3) *Congenital infravesical obstructive lesions in children* In children who are old enough to co-operate in voiding into the uroflometer, useful information can be gained regarding the degree of impairment of voiding velocity Histories of voiding disturbances are also unreliable in these patients and objective evidence is necessary The uroflometer has proven useful in our hands in evaluating problems of enuresis where it may show evidence of early infravesical obstruction when other clinical findings are equivocal The decision to perform cystoscopy can often be made on the basis of abnormal uroflograms

4) *Neurogenic bladder problems* The uroflometer has been an adjunct to cystometry and other tests of neurogenic bladder problems, serving as an additional objective method in following the course of the disease and its response to treatment Since the voiding velocity reflects both detrusor function and infravesical resistance factors, it records the composite aspects of micturition Shields, Baird and McDonald[7] have used this uroflometer to dissociate neurogenic bladder dysfunction from obstructive infravesical disease By comparing the record of the patient's ability to void through a catheter of standard size and the record of his ability to void in a normal manner without a catheter, the effect of the obstructive factor on the urine flow rate can be determined In this way each factor, the bladder force and the bladder outlet, can be investigated

SUMMARY

A new automatic recording uroflometer has been described and the indications for its use have been enumerated No claim is made that the device is capable of precise determinations, but it is sufficiently accurate in testing the velocity of urination in normal and in many abnormal voiding conditions It has many uses in routine office practice in providing a simple, objective, painless test of the patient's voiding problem

435 North Roxbury Drive, Beverly Hills, Calif

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[7] Shields, J R, Baird, R A and McDonald, D F Differential Uroflometry, Paper read at Western Section meeting American Urological Association May 27-30, 1957 Seattle, Washington

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THE HUMAN SIDE OF MEDICINE

CHARLES H. DE T. SHIVERS

It is indeed an honor to address the American Urological Association as President and I would like to thank the members for elevating me to this high office and in addition, express my sincere appreciation to the officers and Executive Committee for their splendid co-operation, along with the Secretary and Executive Secretary (who bear the main burden of the entire organization), and to the chairmen and members of the various committees, appointed and standing, for their valuable assistance.

It has been my privilege, over the years, to listen to many presidential addresses, all of which have been inspiring, but the ones that left the most lasting impressions dealt, at least in part, with the vanishing art of the human side of medicine. Although most of medical science has been acquired recently, the art of healing has been practiced for thousands of years without the benefit of laboratory knowledge. The skill of the ancient physician was largely empirical but permitted him, nevertheless, to formulate prognoses, relieve symptoms, and not uncommonly effect cures. This was an empiricism based on wisdom, experience and knowledge of human nature. While we do not care to return to those times, because of the fabulous advance in medical science, we should, however, in our practice, try to acquire some of this lost art. Howard Rusk,[1] in his article on Chronic Illness and the Medicine of Tomorrow, states, "When the medical student or young physician reaches the point of feeling a deep sense of accomplishment from his efforts to aid the chronically ill and disabled, then he ceases to be a technician and becomes a physician in the true sense of the word, for then he treats people rather than diseases."

As a number of my forebears were members of the medical profession, I have heard many tales relating to their experiences and can recall most vividly my father's life as a physician, who graduated from Jefferson Medical College in 1872 and was engaged in the practice of medicine for a period of 64 years. In the early days, the physician was the most respected member in the community and while he lacked the science of medicine, as we know it today, he was an expert in the art and administered both to the physical and mental ills of the patient. We are all aware of the control of the mind over the body and probably faith, prayer and the doctor represent the combination that brings about the best results. In the early days, the physician had two specifics. One was mercury and the other was quinine, and when these two drugs were not indicated, the patient's recovery depended on supportive treatment, proper nursing and faith—especially faith in his physician, which, when he called, was like a tonic on a spring morning.

In comparing medicine that was practiced by our forefathers and that in

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Presidential address delivered at annual meeting of American Urological Association, Pittsburgh, Pa., May 8, 1957.

[1] Rusk, Howard: Chronic illness and the medicine of tomorrow. J. Chronic Dis., 1: 88–89, 1955.

vogue at the turn-of-the century, we note that it is now a science but was formerly an art The turn-of-the century physician was a beloved, universally respected and influential figure, whereas, at the present time, he is just another professional man, if not, indeed, viewed with suspicion as being too prosperous and hard to obtain for professional advice

The doctor of 1900 learned to depend on his own senses because he lacked the precise diagnostic instruments now available He had to estimate the blood pressure by feeling the radial artery, temperature by touching the brow, and the possibility of diabetic coma by the odor of the breath, thus there developed the skilled artistry of the medical practitioner, which seems so unnecessary today These techniques required direct physician-patient contact which established in a literal as well as a figurative sense, a warm and friendly contact between doctor and patient Today, so many diagnostic methods have been transferred to the laboratory technician and many therapeutic techniques delegated to nurses and "therapists" of various stripes that the physician is more like the operator of a switch board, who inserts his plugs in calling the various departments of the institution or hospital to aid in formulating his diagnosis This is all important but in doing so, he frequently loses the personal touch which means so much in relieving the anxiety of his patient

We should ask ourselves, why so many people are disturbed mentally and what can be done to lessen their tension? In this modern world of ours, some believe that we have gone too far in increasing the anxiety of the population by making them aware of the various diseases which they may contract, by announcements over the radio and television This applies particularly to cancer, which, in some instances, the statements made cannot be substantiated, with the creation of phobias which oftentimes cause as much suffering as the actual disease I am in accord with a recent address by Dr Dwight H Murray,[2] President of the American Medical Association, who states in part "What we need most in medicine today is to find some way of combining modern scientific methods with the personal, friendly touch of the old-time family doctor, who carried only a few medicines in his bag, but in his heart he brought sympathy and personal concern Today, physicians have a tremendous store of knowledge, skills, facilities and drugs, but we have learned that skill and the prescription pad are not substitutes for kindness and understanding We also have learned that fear and anxiety are important factors in all types of illness and these emotional stresses that accompany physical illness should concern the doctor equally as much as the disease itself "

Our failure to administer mental comfort to our patients has been largely responsible for so many people turning to Christian Science, where, we must admit, their physical ills are neglected but their mental ills nurtured Faith is a wonderful asset and faith alone has been responsible for many cures

One of the earliest physicians, who combined religion with medicine, was St Luke, who died nearly 1900 years ago, born a Gentile sometime very near the beginning of the Christian Era, probably, in Antioch of Syria He seems to have been the recipient of the current best culture that the schools of Greek and Roman philosophy and speculation could afford and probably enjoyed citizenship of the Roman Empire. His knowledge of the world of that day was quite comprehensive since he had traveled much and long. He was one of the early converts to the religion of the Nazarenes and, possibly, exerted no little influence in advancing the Christian religion and one of the most potent contributors to the literature of earliest Christianity.

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[2] Murray Dwight H The family doctor (president's address) J A M A , **161** 671–672, 1956

A careful study of his two New Testament writings seems to show that he was as advanced in the diagnosis and cure of diseases as any doctor of his day. Galen, who lived and wrote treatises on medicine some seventy-five years after Luke, uses medical terms that occur in Luke's writings, especially the Gospel. The late Dr. Hobart of London, nearly fifty years ago, in a book entitled "The Medical Language of St. Luke," gives a long list of words which occur solely or chiefly in Dr. Luke's Gospel that are found in Greek medical writings, especially Galen. Luke was very familiar with the classical Greek medical terms used in his time, as both Luke and Galen had studied the same medical textbooks. His greatest and most illustrious-known patient was St. Paul. He became, as it were, his private physician. Behind the great missionary pioneer looms Dr. Luke. He guarded the health of one who, he realized, was turning the world upside down for the cause of universal religion and the expression of spiritual democracy. His personal attachment to St. Paul probably was strengthened by his medical interest in the great man, who, it is generally agreed, suffered from ophthalmia. If Dr. Luke had served only one person and that person the Apostle Paul, it is easy to understand how large a place Dr. Luke, the Evangelist, must cover in the development of the spiritual rights of man; and may no doctor ever forget this thought, and those that combine the healing art with sympathy, kindness and understanding, follow closely in the footsteps of Dr. Luke.

If the young physician is to be properly prepared to solve present-day problems then the medical schools are called upon to include instruction of the effect of these problems on the patient's health. Comprehensive medicine, therefore, should be directed towards the training of the complete physician, preparing him to understand not only the physical ills of the individual but also his personal problems which have a strong influence on his reactions and recovery from these illnesses. The idea is to strive to train a man to be a true physician with broad medical knowledge, scientific and humane in outlook, and able to understand the influence of all extraneous factors upon the making of symptoms.

Some of our eminent members have expressed their ideas regarding the doctor-patient relationship in their presidential address in the following manner.

In 1936, Dr. George Smith[3] in addressing the assembly said in part, "In Urology, Science has advanced and is advancing with rapid strides, yet in no department of medicine is it more essential for the physician to employ his scientific knowledge with Art and to temper it with humanity."

In 1944, Dr. Cyrus Burford[4] advised us in these words: "The urologist of the future must take more time for the individual appraisal of his patient as a personality, and not merely a physical accumulation of functioning organs interrelated "

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[3] Smith, George Gilbert. Presidential address. J. Urol., 36: 599-601, 1936.

[4] Burford, Cyrus E. The urologist of the future (presidential address). J. Urol., 52: 177-179, 1944.

Dr Clyde Deming,[5] in 1946, cautioned us in these words "Science alone is cold, and Science and Art can never be separated in the practice of Medicine on humans Urology demands that the physician practice the Art as well as the Science of Medicine, for all patients with genitourinary lesions require the profession's sincerest consideration "

In 1954, Dr Horatio N Dorman's[6] address, "Where Are We Going?", read before the Mid-Atlantic Section of the American Urological Association, dealt in part with the Art of Medicine, stressing the rapid advancement in the science of medicine but to a large degree the loss of the Art He advocated "considering Art in its true medical sense in order that we may more clearly appraise its importance in the future conduct of our practice of medicine and surgery in the hope that each of us may do his part to help restore the proper human relationship between doctor and patient "

It has been pointed out in a recent paper entitled The Doctor, His Patients and the Illness, by Dr Michael Balint[7] of London, "that the most frequently used drug in general practice is the doctor himself and that this is a drug without pharmacology, without directions as to the dosage, form and frequency of administration, and without leads to the hazards, allergic response or undesirable effects We know that the doctor himself is an extremely powerful drug and that those who use it relieve more suffering than has yet been recorded by the most potent drug in the pharmacopeia The family doctor of old knew this to be so and prescribed himself in generous doses " It would be well for us to recapture this art and to re-establish a close relationship between doctor and patient, for in so doing, we would be administering not only to the body but to the soul and with this close contact, the medical profession would never have to worry about the socialization of medicine

It is more or less common knowledge, today, that every other bed in our nation, at the present time, is allotted to the care of the mentally ill, therefore, it is a problem to which we should give serious consideration Dr Carl Rusche,[8] in his presidential address in 1950 "Not by Medicine Alone", left this thought with us "We should not underestimate the intimate relationship between God and Nature Hope and the power of prayer may be a major contributing factor to the healing process " Our advanced scientific knowledge should be combined with the Art of Medicine as practiced by our former great physicians, and, with God's help, we could improve the lives of many of these people distressed in mind and body

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[5] Deming, Clyde L The status of urology and the urologist following two world wars (presidential address) J Urol , 56 613–618, 1946

[6] Dorman, Horatio N Where are we going? Presidential address, Mid-Atlantic Section of the American Urological Association, April 21–24, 1954

[7] Balint, Michael The doctor, his patients and the illness Quoted from an article written by Dr Francis J Braceland in the May 11, 1956 issue of PHILADELPHIA MEDICINE

[8] Rusche, Carl Not by medicine alone (presidential address) J Urol , 64 441–444, 1950

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UNILATERAL RENAL DISEASE AND HYPERTENSION USE OF THE RADIOACTIVE DIODRAST RENOGRAM AS A SCREENING TEST

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In previous papers[1, 2] the radioactive diodrast renogram was introduced as a new renal function test for measuring individual renal vascular capacity, tubular cell function and ability of the upper urinary tract to evacuate urine The test is performed externally, using two sets of gamma-radiation detection and recording equipment (one for each kidney) following an intravenous injection of diodrast-I^{131} in tracer doses (1 0 μc/5 kg)

Preliminary findings indicated that this test might be a simple, painless and accurate method for screening groups of hypertension patients to discover the few who have unilateral renal dysfunction as the cause of their disease[1, 2] While patients with *abnormal* renograms would then need extensive urological examinations, those with *normal* renograms might be spared the discomfort and expense of such additional tests in most instances

It is the purpose of this paper to describe and evaluate the clinical use of the radioactive diodrast renogram in studying a group of 44 hypertensive patients

CONCEPT OF RENAL HYPERTENSION

Goldblatt (1934)[3] found that partial occlusion of one renal artery produced hypertension in dogs Page and Corcoran (1948)[4] encased dogs' kidneys in silk or cellophane producing a constricting, fibrotic renal capsule The cause of experimental hypertension was thought to be due to renal ischemia Numerous clinical investigators have reported hypertension in patients with renal ischemia due to infarcts, varying degrees of arterial occlusion, fibrotic inflammatory reactions and obstructive uropathy Successful relief of hypertension has followed nephrectomy for unilateral renal disease or corrective surgery for bilateral renal arterial defects Still, the number of patients with undisputed primary "renal hypertension" cured by surgery is small[5] It is estimated that two to five per cent of hypertensive patients may have unilateral renal disease as the etiology of their disease

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Read at annual meeting, American Urological Association, Pittsburgh, Pa , May 8, 1957

Note by editor Doctor Winter's paper was awarded a prize in the essay competition sponsored annually by the American Urological Association's Committee on Scientific Research, Dr Miley B Wesson, chairman

[1] Taplin, G V , Meredith, D M , Kade, H and Winter, C C The radioactive renogram J Lab & Clin Med , **48** 886, 1956

[2] Winter, C C A clinical study of a new renal function test The radioactive diodrast renogram J Urol , **76** 182–196, 1956

[3] Goldblatt, H , Lynch, J , Hanzal, R F and Summerville, W W Studies on experimental hypertension I Production of persistent elevation of systolic blood pressure by means of renal ischemia J Exp Med , **59** 347–379 1934

[4] Page, I H and Corcoran, A C Experimental Renal Hypertension Springfield, Ill Charles C Thomas, 1948

[5] Smith, Homer Unilateral nephrectomy in hypertensive disease J Urol , **76** 685–701, 1956

The accepted method for demonstrating unilateral kidney dysfunction is by using one or more of the standard individual renal clearance tests (i e, para aminohippuric acid, inulin, creatinine, and diodrast) [6] Howard and others (1954)[7] and Poutasse and Dustan (1956)[8] suggested measuring sodium concentration, osmolarity and urine volume from each kidney as a means of detecting the offending kidney Poutasse (1956) recently emphasized the value of aortography in visualizing renal arterial lesions

From this brief background it seems clear that there is need for a simple, accurate, non-traumatic *screening test* to estimate individual renal vascular capacity and functional abnormalities in hypertensive patients, especially in children and young adults

METHOD OF STUDY

The radioactive diodrast renogram* was used to estimate individual renal function in 44 hypertensive† patients of both sexes and various ages Concurrently, the author and various members of the medical and urological house staff performed one or more of several standard renal function tests The latter included retrograde ureteral catheterization for standard individual renal clearance tests, excretion of phenolsulfonphthalein and/or indigo carmine, excretory urography, aortography and the determination of blood urea nitrogen and creatinine

The renogram was performed as previously described [1] [2] Briefly, an intravenous injection of a 1 $\mu c/5$ kg dose of diodrast-I^{131}‡ was followed by continuous external measurements of the changing radioactivity levels over each kidney area for 10–30 minutes using gamma-ray scintillation detectors and Esterline-Angus recorders to register the data in the form of permanent tracings In this graphic record, the initial spike (a) represents the first flood of the radioactive agent through the vascular network of the kidney and adjacent tissue The height of the spike is an index of the capacity of the renal arterial system (figure 1, right kidney) The steepness and height of the secondary rise in the tracing (b) reflects the quality of tubular cell secretory function, but may be modified by urinary stasis in some instances The final drop in the tracing (c), which normally is an index of the ability of the upper urinary tract to evacuate urine, may be delayed by urinary stasis or occasionally by tubular cell dysfunction

RESULTS

Pertinent data obtained from the 44 individuals studied in this series were tabulated and divided into three groups according to the renogram results

[6] Smith, Homer The Kidney Structure and Function in Health and Disease New York and London Oxford University Press, 1951

[7] Howard, J E, Berthrong, M, Gould, D M and Yendt, E R Hypertension resulting from unilateral renal vascular disease and its relief by nephrectomy Bull Johns Hopkins Hosp, 94 51–85, 1954

[8] Poutasse, E F and Dustan, H Urologic causes of hypertension I Hypertension due to renal artery lesions Cleveland Clinic Quart, 23 3–15, 1956

* The radioactive diodrast renogram will be called the renogram throughout the remainder of this paper

† Hypertension in adults is defined as a consistent diastolic blood pressure of 95 or more mm of mercury

‡ Obtained from the Abbott Laboratories, Oak Ridge, Tennessee

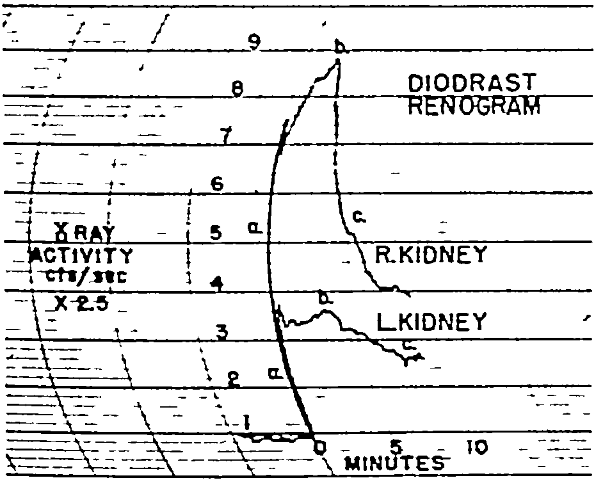


FIG 1 Left renal vascularity (a) and function (b) markedly reduced in contracted pyelonephritic kidney

unilateral abnormal renogram, bilateral abnormal renograms and bilateral normal renograms

Unilateral abnormal renogram Ten hypertensive patients (table 1) had an unilateral abnormal renogram All patients except two were less than 50 years old The diagnoses of the abnormal sides as made by excretory and retrograde urography and aortography were contracted pyelonephritic kidney (2), coarctation of renal artery, circoid aneurysm of renal artery, postoperative partial renal infarction, hydronephrosis due to ureteral stricture, hydronephrosis due to ureteral calculus, agenesis of kidney, partially calcified kidney and surgically absent kidney with bladder neck obstructive uropathy All of the patients were thought to have hypertension on the basis of these disorders Seven of these patients had surgical procedures in an attempt to correct the primary disease and/or the hypertension The postoperative blood pressures are recorded in the table

The excretory urogram revealed unilateral renal disease in nine of the patients, being normal bilaterally in one

Indigo carmine (4 patients), phenolsulfonphthalein (4 patients) and creatinine clearance tests (3 patients) were abnormal for one side only in all cases where used

Sodium concentration (3 patients) and urine volumes (4 patients) were abnormal unilaterally in all cases where measured

Inulin and para-aminohippuric acid clearance rates were abnormal unilaterally in the only patient where used

Aortography was attempted in seven individuals and was successfully carried out in six It showed unilateral abnormality in all instances and revealed the primary disorder in two In one patient the aortogram did not reveal the true vascular capacity of the abnormal kidney

When all of the standard split renal function tests were evaluated and compared with the renogram, excellent correlation was found

TABLE 1 *Hypertensive patients with unilateral abnormal renograms*

Patient Sex/Age	Diagnosis	Blood Pressure	Blood Urea Nitrogen	Serum Creatinine	Radioactive Diodrast Renogram	Excretory Urogram	Retrograde Pyelogram	Aortogram	Standard Renal* Function Tests	Right Kidney	Left Kidney	Renogram Correlation	Treatment	Follow up Blood Pressure
1 H B M 59	Partially calcified L kidney	220/120	17	1 2	↓ L vascularity and function R normal	Partially calcified L kidney & ↓ medium R normal	Same as IVP	↓ vascularity L kidney R normal	Volume PSP Creatinine Sodium PAH Inulin	3 7 10 80 20 213 63	0 8 2 (10′) 14 17 50 12	Good	Left nephrectomy	140/80 2 months
2 A K F 13	Partial infarction L kidney	150/116	15	1 2	↓ L vascularity and function. R normal	Left hydronephrosis post op pyeloplasty R normal	Same as IVP	↓ vascularity L kidney R normal	Volume PSP Creatinine Sodium Indigo	0 68 30 76 35 Normal	0 38 10 (15′) 64 14 Delayed & poor concentr	Good	Observation	130/80 12 months
3 B T F 24	Coarctated R renal artery	230/130	14		↓ & delayed R function L normal	Both normal	Same as IVP	Coarctated R renal artery L normal	Volume PSP	0 1 0	1 75 20 (20′)	Good	Resection of coarctated R. renal artery	130/80 12 months
4 M M 41	Circoid aneurysm R renal artery	240/130	14		↓ R vascularity and function L normal.	Contracted R kidney Left normal	Same as IVP	Circoid aneurysm R renal artery L normal	Volume Creatinine Sodium	0 2 36 3	0 54 130 17	Good	Right nephrectomy	170/100 12 months
5 B E M 1½	Contracted pyelonephritic L kidney	148/92	11	1	↓ L vascularity and function R normal	No medium L kidney R normal	Contracted pyelonephritic L kidney R. normal	L renal artery not filled Right normal	Indigo Unable to catheterize left ureter for tests	Normal	Delayed & poor concentr	Good	Left nephrectomy	90/50 12 months

6 C C M 33	Agenesis I kidney	250/105	21		Absent or nonfunctioning I kidney R normal	No medium I kidney R normal	Unable to catheterize L ureter R normal	Left renal artery not filled R. normal	Indigo Unable to catheterize left ureter	Normal	0	Good	Resection of vestigial L kidney	150/88 15 months
7 A L M 48	Contracted pyelonephritic R kidney	280/100	15	1 1	↓ R. vascularity and function I normal	Contracted right kidney I normal		Unsuccessful	PSP	0	13 (20)	Good	R nephrectomy deferred due to lung tumor	280/100 1 months
8 H F M 32	R hydronephrosis (stricture)	150/100	13		↓ R vascularity and function and drainage I normal	R hydronephrosis. I normal						Good	Observation	
9 D F M 47	I hydronephrosis (calculus)	150/100	11	0 0	↓ I vascularity function and drainage R normal	I hydronephrosis R normal	Same as IVP					Good	Left ureterolithotomy	130/90 15 months
10 J O M 60	Surgically absent I kidney and prostatic obstruction	180/100	15	1 2	Absent or nonfunctioning L kidney R normal	No medium I kidney R normal						Good	Retropubic prostatectomy	110/70 15 months

* Volumes para aminohippuric acid inulin and creatinine are ml/minute phenolsulfonphthalein is per cent and sodium is milliequivalents per liter ↓ = decreased

The following 2 cases illustrate the value of the renogram in detecting unilateral renal disease amenable to surgical treatment for hypertension

Case report B E (H H No 99465), a 19-month-old white boy, was noted to have persistent hypertension (140/92) for 9 months He was first seen at 6 months of age during an attack of acute gastroenteritis accompanied by sepsis, oliguria and transient coma Urinalysis showed pyuria Subsequent urological examination revealed a poorly functioning, pyelonephritic left kidney

After intravenous injection, indigo carmine appeared late and in poor concentration from the left ureteral orifice while retrograde pyeloureterography ruled out ureteral obstruction The renal function and pyelogram of the right kidney were normal Aortography further implicated the left kidney by failing to outline the left renal artery

The baby was sedated with chloral hydrate and five microcuries of diodrast-I^{131} was injected intravenously to initiate a renogram test As seen in figure 1, the right renogram appeared normal while the left tracing reflected marked diminution in (a) renal vascular and (b) functional capacity As a result of these tests, the small left pyelonephritic kidney was removed The blood vessels were small but patent Postoperatively, the blood pressure declined and has remained around 90/50 mm of mercury for 12 months

In this instance the renogram correlated well with the anatomical findings, proving more accurate than the aortogram or intravenous urogram

Case report B T (U H No 011-39-41), a 24-year-old-white woman was admitted to the hospital in her third prenatal month with a blood pressure of 200/130 mm mercury Her blood urea nitrogen was 14 mg per cent An intravenous urogram revealed a small left calyceal diverticulum containing gravel and otherwise normal upper urinary tracts These findings were confirmed by retrograde studies The left kidney excreted 20 per cent phenolsulfonphthalein in 35 ml in 20 minutes, the right kidney only 2 ml with no phenolsulfonphthalein Other tests performed were blood adrenalin, 5 4 micrograms (normal), urinary catechols, 160 micrograms (normal), regitine and benzodiozane tests (normal) An aortogram (fig 2) revealed a coarctated right renal artery A renogram was performed showing marked diminution and delay of right renal function while the left renogram was normal (fig 3, *A*) On the basis of these tests it was felt that the coarctated right renal artery was producing right renal ischemia resulting in hypertension The coarctated segment of the right renal artery was resected and for 12 months the blood pressure has remained normal (around 130/80) A 9-month postoperative renogram (fig 3, *B*) has returned entirely to

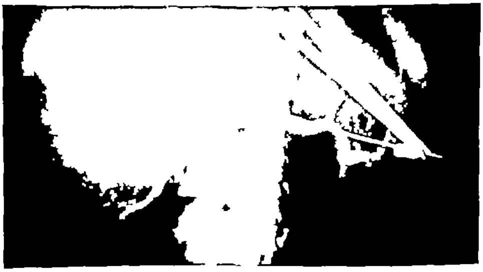


FIG 2 Coarctated trunk of right renal artery (through courtesy of Dr Donald Burke)

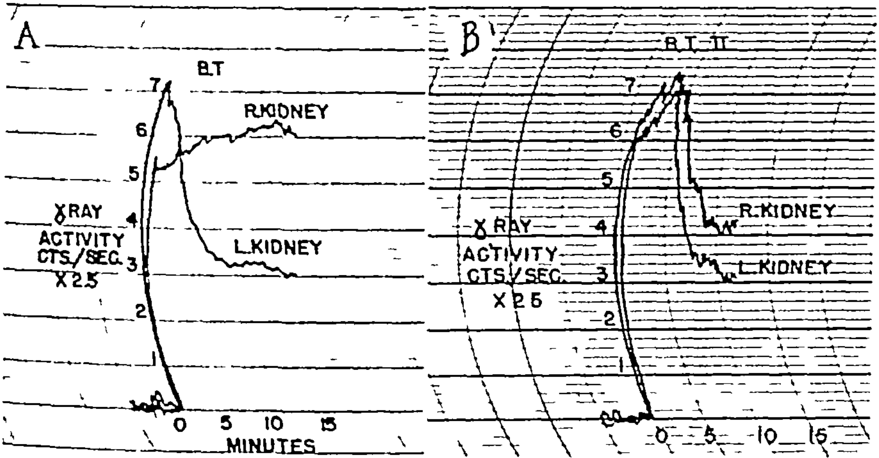


Fig 3 A, preoperative right renogram shows decreased and delayed function B, post operative renogram has returned to normal

normal, correlating well with the normal blood pressure In retrospect, it is felt that the lack of excretion of phenolsulfonphthalein from the right kidney was misleading while the renogram and excretory urogram accurately showed that function was present

Bilaterally abnormal renograms Twenty-five patients had bilaterally abnormal renograms Seven had split phenolsulfonphthalein tests performed showing good correlation with the renogram Endogenous creatinine clearance in 4 patients compared well with the renogram in two Bilateral renal sodium measurements in 3 patients correlated well in two

Twenty excretory urograms were performed in this group All but three correlated closely with the renograms It was interesting to note that those three patients were all in the seventh decade of life Previous studies[1, 2] have indicated that nonhypertensive individuals in this age group may have apparently normal excretory pyelograms but definitely abnormal renograms

The following case report illustrates an instance where the screening renogram appeared abnormal bilaterally and could have saved further urological investigation

Case report A 5½-year-old white boy was found to have bilateral flank masses at 7 months of age The blood pressure gradually rose to 210/150 mm /mercury The boy was given serpasil, reducing the blood pressure to 180/110 The nonprotein nitrogen was 54 mg per cent An intravenous urogram revealed decreased concentration of contrast medium bilaterally but outlined renal architecture compatible with a diagnosis of polycystic disease The renogram correlated closely with these findings showing bilateral diminution of vascular capacity and tubular cell function (fig 4)

Bilaterally normal renograms Nine hypertensive patients had normal renograms Their other renal studies were also normal, showing good correlation The case to follow illustrates that a normal renogram could make further urological examinations unnecessary

Case report J T, a 32-year-old white man, acquired chronic myelopathy

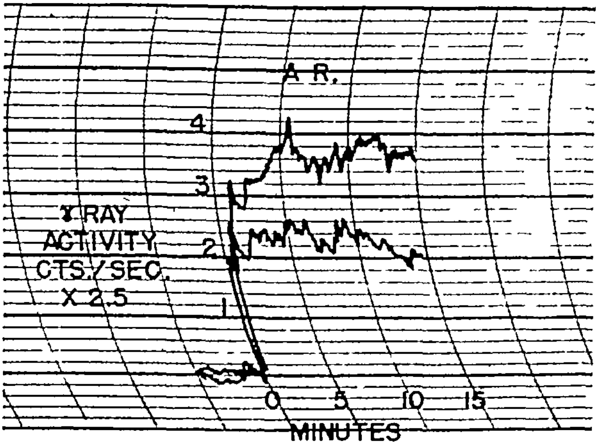


FIG 4 Bilaterally abnormal renogram shows diminished vascularity and function due to polycystic renal disease

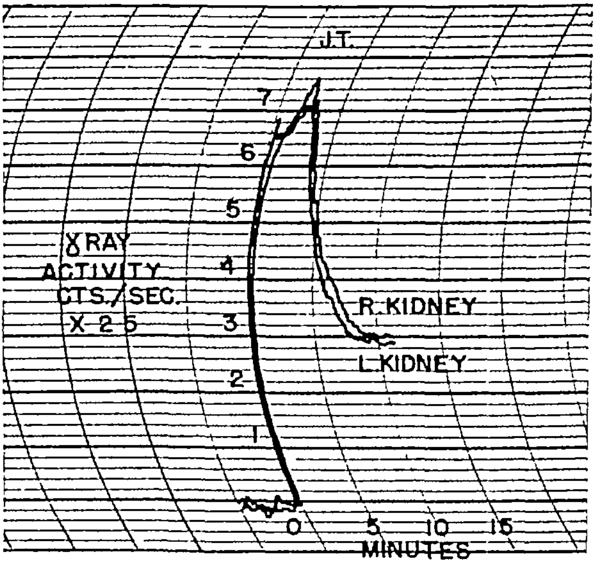


FIG 5 Bilaterally normal renogram

below the seventh thoracic spinal level following a gunshot wound 10 years previously His blood pressure was consistently recorded at a level of 140/95 Urinalysis was normal except for moderate proteinuria An intravenous pyelogram and the blood urea nitrogen were normal The screening renogram (fig 5) was also normal Further urological examinations were considered unnecessary in his case

DISCUSSION

The results obtained in this study demonstrate, in general, that good correlation exists between the renogram and the findings from a battery of standard methods of determining renal function

Conversely, certain deficiencies of the excretory urogram as a single index of renal function were shown (4 out of 30 urograms misleading) Also, when one kidney continues to function normally, blood chemistry studies have little diagnostic value in revealing renal dysfunction

The excellent correlation between the renogram and other split renal function tests (over 90 per cent) demonstrates that *the renogram has considerable potential value in screening hypertensive patients for unilateral renal dysfunction* It should be particularly useful in hypertensive children and young adults, to discover those with remedial unilateral renal disease

The renogram is unique among kidney function tests in that it measures three functions which are related to the etiology of "renal hypertension" (a) renal vascularity, (b) renal tubular cell function, and (c) upper urinary tract stasis Furthermore, from the renogram, it is possible to cross-compare individual kidney functions directly, thereby identifying the diseased kidney

The advantages and disadvantages of the renogram have been tabulated previously * However, its advantages which apply especially to hypertensive patients are first, it is nontraumatic, second, it does not affect kidney function or renal blood flow, and third, it may be performed safely in patients too ill to undergo retrograde pyelography and under circumstances, especially in children, where surgical procedures are not advisable

Arteriography is the only nonsurgical method available for visually localizing renal vascular lesions, such as congenital defects of the renal artery or its branches The renogram may indicate vascular deficiency and functional impairment, but it does not localize the site or reveal possible causes of renal vascular lesions While the renogram is more simple, less hazardous and provides more data on renal functions (three main renal functions) than the aortogram, arteriography should still be used in most cases when studying hypertensive patients if the possibility of renal ischemia exists

Occasionally, technical difficulties prevent the aortogram from outlining renal vascular defects This occurred in two patients in this study By contrast, the vascular segments of the renograms accurately indicated the patients' true renal vascular status in both cases In the other patients the aortograms and the vascular segments of the renograms showed good correlation

In this study the nine hypertensive individuals with normal renograms also had normal values with standard renal function tests including intravenous urograms Thus, *most persons with normal renograms could be spared the discomfort, time and expense of extensive urological investigation*, which may include one or more of the following anesthesia, cystoscopy, retrograde ureteral catheterization, and individual renal clearance tests and aortography More complete investigation would be indicated of course if the renogram revealed unilateral renal abnormality

Suggested plan for investigating hypertensive patients From the results of this preliminary study the following plan is offered for evaluating hypertensive patients

1 Obtain a pertinent history and perform a careful physical examination including special examinations to rule out acute and chronic glomerulonephritis,

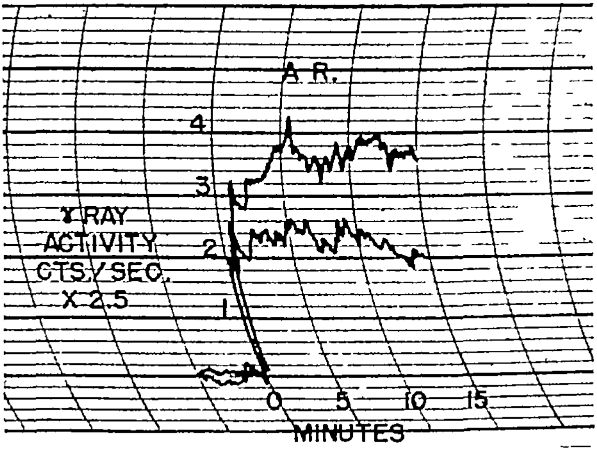
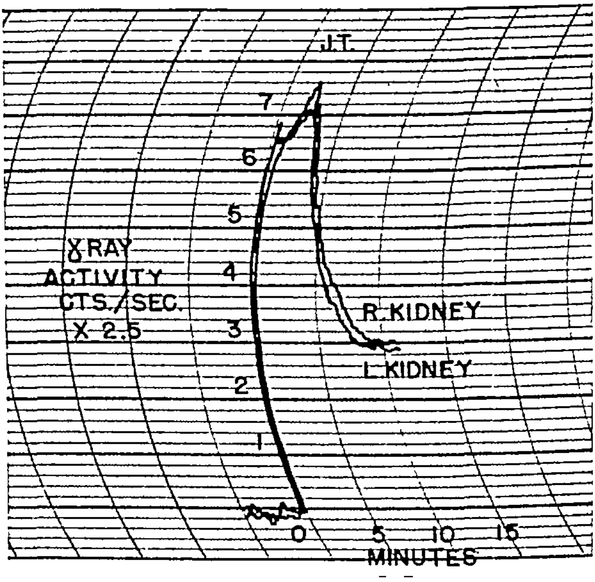


FIG 4 Bilaterally abnormal renogram shows diminished vascularity and function due to polycystic renal disease



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The excellent correlation between the renogram and other split renal function tests (over 90 per cent) demonstrates that *the renogram has considerable potential value in screening hypertensive patients for unilateral renal dysfunction*. It should be particularly useful in hypertensive children and young adults to discover those with remedial unilateral renal disease.

The renogram is unique among kidney function tests in that it measures three functions which are related to the etiology of "renal hypertension": (a) renal vascularity, (b) renal tubular cell function, and (c) upper urinary tract stasis. Furthermore, from the renogram, it is possible to cross-compare individual kidney functions directly, thereby identifying the diseased kidney.

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Occasionally, technical difficulties prevent the aortogram from outlining renal vascular defects. This occurred in two patients in this study. By contrast, the vascular segments of the renograms accurately indicated the patients' true renal vascular status in both cases. In the other patients the aortograms and the vascular segments of the renograms showed good correlation.

In this study the nine hypertensive individuals with normal renograms also had normal values with standard renal function tests including intravenous urograms. Thus, *most persons with normal renograms could be spared the discomfort, time and expense of extensive urological investigation*, which may include one or more of the following: anesthesia, cystoscopy, retrograde ureteral catheterization, and individual renal clearance tests and aortography. More complete investigation would be indicated of course if the renogram revealed unilateral renal abnormality.

Suggested plan for investigating hypertensive patients. From the results of this preliminary study the following plan is offered for evaluating hypertensive patients.

1. Obtain a pertinent history and perform a careful physical examination including special examinations to rule out acute and chronic glomerulonephritis,

coarctation of the aorta, pheochromocytoma, periarteritis nodosa and pituitary-adrenal disease

2 Perform the radioactive diodrast renogram

3 If the renogram reveals unilateral abnormally, a urological investigation plus an aortogram is indicated with few exceptions

4 Where surgery is contemplated, conventional individual renal clearance tests may be performed to compare with the renogram

SUMMARY

The renal status of 44 hypertensive patients was evaluated by one or more standard individual renal function tests and the radioactive diodrast renogram Excellent agreement was shown to exist

In 10 patients the renogram gave information indicating *unilateral* renal disease This information plus that gained from conventional studies led to surgical treatment in seven

Nine of the 44 patients studied had normal renograms bilaterally and no evidence of renal disease by standard methods of examination

Twenty-five patients were found to have abnormal renograms bilaterally These patients had bilateral renal disease demonstrated by one or more standard methods

CONCLUSION

The use of the radioactive diodrast renogram as a rapid screening procedure for detecting unilateral renal disorders in hypertensive patients has been shown to have merit From data on the 44 patients presented the renogram has been shown to be a highly reliable method for detecting disorders of the individual kidney However, this study is not sufficiently comprehensive to permit exact evaluation of its reliability in detecting all causes of renal hypertension These preliminary results have encouraged us to continue and enlarge the scope of this medical-urological investigation of renal hypertension, particularly in children and young adults

This study has also demonstrated the need for a co-operative program of investigations, requiring the combined efforts of the internist and the urologist to ensure an accurate diagnosis and effective therapy in these patients It is felt that the routine use of the renogram as a screening test in such a program will provide the simple, painless diagnostic tool which has not been available previously

The author is deeply appreciative of the following for their generous donation of aid and consultation Dr George V Taplin, Atomic Energy Project, U C L A , Dr Willard E Goodwin, professor of urology, U C L A , Dr R L Bennett, Radioisotope Department, U C L A , Dr Morton Maxwell, Renal Clinic, U C L A , the resident staffs of Wadsworth Veterans Hospital, University of California Hospital, Harbor General Hospital and Long Beach Veterans Hospital, and Mr William Martinsen of the Veterans Administration Medical Illustration Department, Los Angeles

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PHYSIOLOGY OF THE HUMAN SOLITARY KIDNEY

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This research was undertaken to evaluate glomerular and tubular function of the healthy, congenitally solitary kidney in young adults and to measure effective renal blood-flow through such kidneys. No such information has been available so far as we know. The data from the congenitally solitary kidney are compared with those from the healthy kidney which had become hypertrophied secondary to surgical removal of its mate. The information is correlated with available data on the anatomical constitution of the congenitally solitary kidney.

Those with a congenitally solitary kidney were grateful when informed that they had only one kidney, which was working as well as two, and that they should take special care to avoid injury.

THE PATIENTS AND METHODS

1. The patients (see also table 1). *VAH 44070* was a well developed man admitted for "pain" in the left epididymis. Both epididymides were clinically normal. His arterial pressure was 115/80. A right hypertrophied, congenitally solitary kidney was indicated by routine intravenous pyelography and confirmed by aortography (fig. 1) and cystoscopy. Urine from the kidney showed no growth upon culture. He had mild posterior urethritis secondary to Staphylococcus aureus. *VAH 53860* was a well developed man with a hypertrophied solitary right kidney, confirmed by aortography. Four months before the study he presented himself anuric for several hours, whereupon an obstructing calculus was removed surgically from his right ureter. Recovery was smooth. Subsequent pyelography showed no hydronephrosis or pyelectasia. Concentration of urea-nitrogen in his blood at time of study was 13 mg. per 100 cc. *VAH 54247* was a well developed man with mild posterior urethritis. His arterial pressure was normal. The only significant findings were a hypertrophied right kidney and a remarkably hypoplastic left kidney (fig. 2). Both kidneys concentrated urokon equally by intravenous pyelography (fig. 2, *C*) and yielded prominent nephrograms (fig. 2, *B*) immediately after intra-aortic injection of urokon (fig. 2, *A*). The left renal artery, *la*, was conspicuously narrow and the right renal artery, *ra*, was enlarged. *VAH 12639* underwent left nephrectomy 8 years previously for "idiopathic hematuria." No significant abnormality was found in the excised kidney other than hyperemia and inflammation of the papillae, possibly due to the repeated retrograde pyelography (Army Medical Museum Acc. No. 176826). He had sicklemia and a hypertrophied right kidney. Otherwise he appeared urologically sound. *VAH 55207* was a well developed man who had undergone left nephrectomy 6 years previously for "serious infection." He presented himself for urological evaluation and was found sound. Culture of catheterized urine

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yielded nothing He had a hypertrophied right kidney *VAH 52688* was a well developed man who had undergone right nephrectomy for hypernephroma 2 years previously He had a hypertrophied left kidney and no evidence of cancer Aortography disclosed the typically widened renal artery *VAH 43197* was a well developed man who had undergone left nephrectomy 5 years previously for stones His arterial pressure was 110/70 and he was urologically sound except for low grade chronic prostatitis He had an enlarged myocardium secondary to old rheumatic heart disease and he had recovered from a myocardial infarct *VAH 47023* had undergone left nephrectomy 6 months previously for hypernephroma He appeared urologically sound, without evidence of cancer His arterial pressure was 116/60 *VAH 32130* was a slender man who underwent right nephro-ureterectomy 1 year previously for transitional cell carcinoma of right ureter A minor infarct of the left kidney occurred shortly after operation and resulted in anuria until removal of the blood clot from the renal pelvis by pyelotomy after 24 hours Thereafter his recovery was uneventful At time of study he had put on weight and had no sign of cancer *VAH 45848* was a well developed man who presented himself with gross hematuria Intravenous pyelography showed good concentration bilaterally He underwent right nephrectomy for hypernephroma 3 weeks before the present study

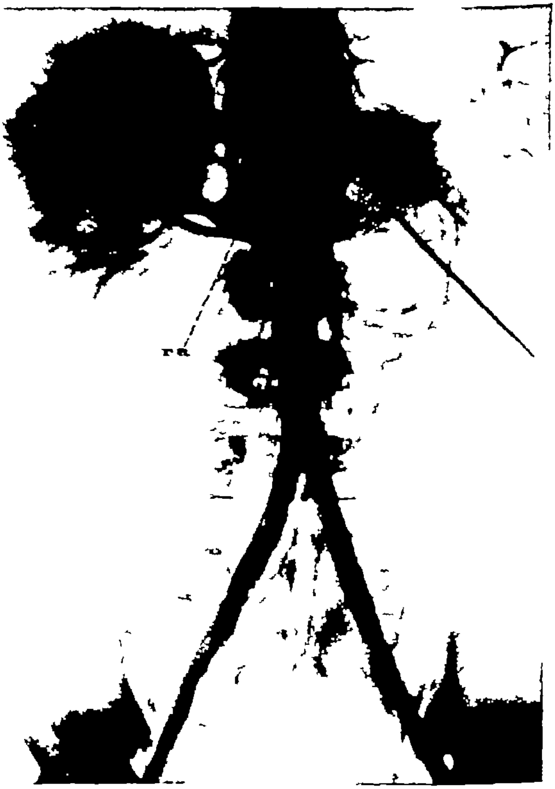

FIG 1 Translumbar aortogram of patient VAH 44070 *ra* Artery to congenitally solitary right kidney

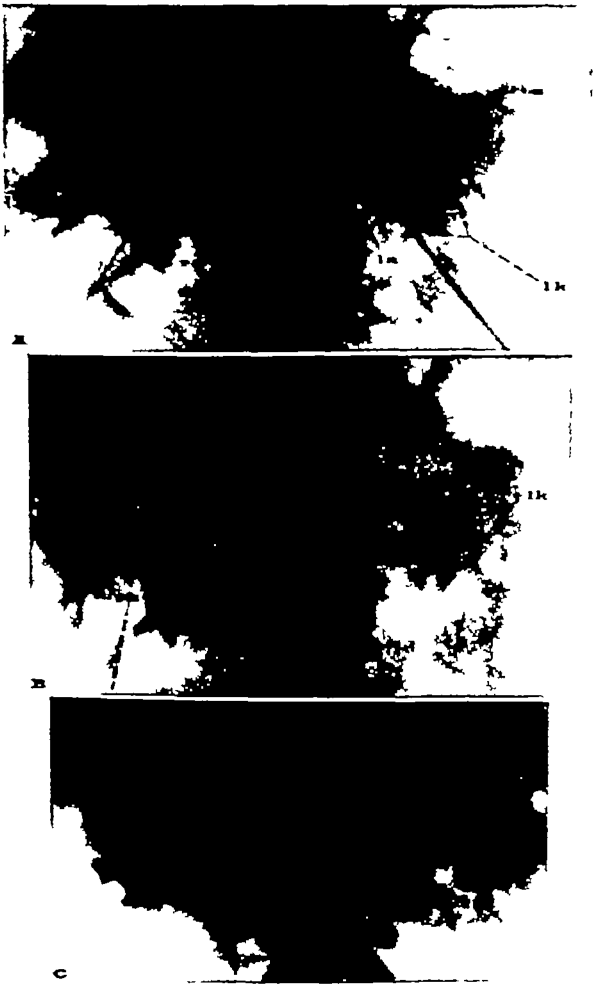

FIG 2 A translumbar aortogram of patient VAH 5-2-7 with hypertrophied right kidney and hypoplastic left kidney (see text). *la* Left renal artery; *ll* shadow of left kidney; *ra*, right renal artery.

B radiogram taken immediately after above aortogram. *ll* shadow of left kidney, *rl* shadow of right kidney.

C intravenous pyelogram of same patient. Note good concentration of iodide on left kidney, *ll*.

2 *Clearance technique*.* Glomerular filtration rate (GFR) was the inulin-clearance. Inulin was measured according to Roe et al. (49). Effective renal plasma-flow (ERPF) was the number of cubic centimeters of plasma cleared of para-aminohippurate (PAH) per minute at low plasma-levels of PAH. PAH was measured by the method of Smith et al. (55). Effective renal blood-flow = ERPF/1 minus the hematocrit, in which the hematocrit is expressed as a fraction of one. Tubular excretory mass (Tm) was the maximal rate of tubular excretion of PAH (in mg. per minute) after raising the plasma-level of PAH to a high requisite level. This

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* For details and discussion see [illegible] monograph.

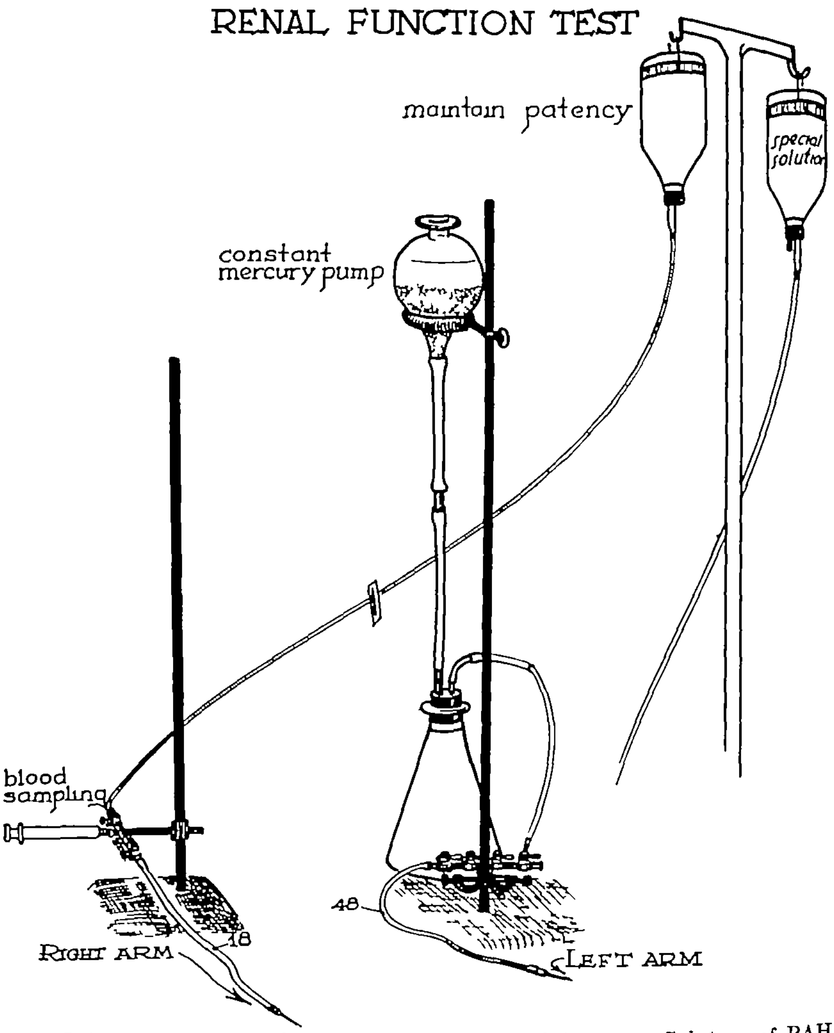

FIG 3 Infusion equipment for measurement of renal function Solution of PAH an inulin is in Erlenmeyer flask and is infused into left arm, through a No 20 needle, by stead drip, at 4 cc/min, of mercury through a No 27 needle "Special solution" may be infuse by attaching to one of the stopcocks of the manifold, no such solution was used in th present research Short No 18 needle in right arm is kept patent by 5 per cent dextrose i water containing heparin and is used for drawing blood sample through manifold

Maximal amount of PAH excreted per min − amount of PAH filtered pe
minute = maximal amount excreted by the tubules per min (or TmPAH)

For the measurement of clearances, the subject was recalled several week after the diagnostic study including translumbar aortography After fastin overnight with a sound sleep in the hospital, he was wheeled into a quiet roo without breakfast and a schedule exemplified thus was followed

6 a m An 18F balloon catheter was inserted and left indwelling with 10 cc i the balloon

7 to 7 15 a m The patient drank 1,000 cc of water

7 30 a m The inulin was dissolved by boiling

8 a m ('0' time) 1 Ten cc of blood were drawn in a syringe with heparin for the PAH and inulin blanks

2 Intravenous infusion was given in both arms (fig 3)

(a) Infusion for sample arm 5% dextrose in water containing 5,000 units of heparin This was to maintain patency of the needle (fig 2)

(b) Infusion by mercury gravity pump

Inulin* 70 cc (10%)
PAH† 20 cc (20%)
Distilled water q s to 500 cc
} to run at 4cc/min

3 Intravenous priming with

Inulin 30 cc (10%)
PAH 4 cc (20%)
Wait 30 minutes Discard urine passed in this interval
Wash bladder with 100 cc water and discard

4 Begin "runs" for measurement of GFR and ERPF Note time Each run of urine collection is 10 minutes

(a) Draw 11 cc blood Label B_1 Note time

(b) At 7 minutes introduce 50 cc water and about 50 cc air into bladder through the catheter Clamp off catheter

(c) At 9 minutes introduce another 50 cc water and about 50 cc air into bladder and clamp catheter

(d) Empty bladder at 10 minutes Label U_1

(e) Draw 11 cc blood Label B_2 Note time

(f) Start new urine collection Repeat procedure above Empty bladder at 10 minutes Label U_2

(g) Draw 11 cc blood Label B_3 Note time

(h) Repeat one more run Measure urine sample of each run in graduated glass cylinder subtract 100 cc (dilution amount introduced) and record reading Dilute to 250 cc or, if total volume is greater than this, dilute to 500 cc

5 Begin "runs" for measurement of tubular excretory maximum for PAH, i e TmPAH

(a) Change mercury gravity pump infusion to second flask containing

Inulin 70 cc (10%)
PAH 250 cc* (20%) to run at 4cc/min
Distilled water q s to 500 cc

(b) Intravenous priming with

Inulin 10 cc (10%)
PAH 60 cc‡ (20%)

3 *Measurement of internal diameter of renal artery was done from trans-lumbar aortograms which were performed with the method previously described by* Maluf and McCoy [illegible] Injection [illegible] at level of T_{12}

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* 50 cc ampoules [illegible]

† 50 cc ampoule has 20% [illegible]

‡ Assumes [illegible]
Thus only 100 cc of PAH [illegible] per 100 cc

There were no untoward effects The diameter of the renal artery was measured close to the aorta with a vernier caliper by a technique to be described (Maluf, '58) The direct measurement was reduced by 10 per cent, which is approximately the radiographic enlargement of a structure at the level of the renal artery in a prone subject

RESULTS

1 *Glomerular filtration rate* (GFR) was 72 5 per cent and 53 5 per cent of normal in the congenitally solitary kidney and in the fully hypertrophied, surgically solitary kidney, respectively (table 1) The difference between the two categories of solitary kidney may be due, at least partly, to difference in average age In the kidney which had been relieved of a functioning mate only 3 weeks before study (VAH 45848), GFR was 45 per cent of normal (table 1) Given that two normal kidneys have 2 4 × 10^6 glomeruli (Kittelson, '17, Vimtrup, '28) and that the normal GFR is 131 cc/min , then every glomerulus of a normal pair of kidneys filters 0 91 × 10^{-6}cc/sec (see also Pappenheimer et al , '51) The average GFR of a congenitally solitary kidney was 95 cc/min (table 1) Given that such a kidney has the same number of glomeruli as a normal single kidney (see *Discussion*), that is, about 1 2 × 10^6, then every glomerulus of such a kidney filters 1 3 × 10^{-6} cc/sec This increase is associated with a larger glomerulus than

TABLE 1

Initials	VAH No	Race	Age	Etiology	GFR	CCr	ERPF	FF	TmPAH	GFR/Tm PAH	ERPF /Tm PAH
Normals (means and standard deviation)*					131± 21.5	150± 20	697± 136	0 19± 0 02	77.5± 12.9	1 7	9 0
F C S	44070	N	28	Congenital	73	88	734	0 10	113	0 64	6 5
LeR C	53860	W	29	Congenital	110	97	663	0 16	87	1 16	7 5
E N J	54247	N	23	Congenital	102	113	554	0 19	97	1 05	5 7
Average	—	—	26	—	95	99	650	0 15	99	0 95	6 6
% of normal	—	—	—	—	72 5	66 0	93 8	79 2	128 0	56 0	73 5
C Y	12639	N	29	Surgical	78	75	637	0 12	132	0 48	4 8
C C B R	55207	W	37	Surgical	79	87	641	0 13	172	0 46	3 7
S C	52688	W	45	Surgical	72	83	881	0 08	73	0 99	12 1
M R	43197	W	48	Surgical	79	96	359	0 22	77	1 09	4 7
E J S	47023	N	52	Surgical	70	77	649	0 11	96	0 72	6 8
C A M	32130	W	59	Surgical	62	60	511	0 12	68	0 90	7 5
Average	—	—	45	—	70	80	613	0 13	103	0 77	6 6
% of normal	—	—	—	—	53 5	53 3	88 5	68 5	134 0	45 3	73 5
M C S	45848	W	42	Surgical (3 weeks)	59	63	429	0 14	60	0 70	7 1
% of normal	—	—	—	—	45 0	42 0	61 8	73 8	77 5	41 0	78 0

* From H W Smith Lectures on the Kidney Lawrence, Kansas Univ Extension Division 134 pp 1943

normal * The filtration-rate per glomerulus is almost identical in all mammals for which it has been calculated man, dog, cat, rat (Pappenheimer et al) Its higher value in the hypertrophied solitary kidney is probably secondary to the almost doubling of blood-flow per nephron of such a kidney

2 *Clearance of endogenous creatinine* (C_{cr}) is roughly equal to the GFR (table 1)

3 *Effective renal plasma flow* (ERPF) through the congenitally or surgically solitary kidney tends to be somewhat less than through a pair of normal kidneys (table 1) The lower value for the surgically solitary kidney is probably due to the higher average age of the subjects with the acquired solitary kidney (table 1) Rise in *effective* renal plasma-flow must await growth of renal tubular mass This is exemplified in a healthy kidney studied only 3 weeks after removal of its functioning mate (see below under *Tubular maximum*) The *actual* renal blood-flow, however, may have risen shortly after contralateral nephrectomy

4 *Filtration-fraction* (FF) or the fraction of ERPF filtered (=ERPF GFR) tends to be abnormally low in both the congenitally and surgically solitary kidney (table 1) The cause for this is unknown It does not appear valid to postulate that the renal capsule causes rise in intrarenal pressure by limiting free expansion of the enlarging kidney The FF is low even in the congenitally solitary kidney, in which the renal capsule doubtless becomes deposited in accordance with growth of the kidney during embryonic development

5 *Tubular maximum* (Tm) for para-aminohippurate (TmPAH) is actually greater in the congenitally or the surgically solitary healthy kidney than in a pair of normal kidneys combined (table 1, fig 4) The magnitude of TmPAH is essentially identical in both types of solitary kidney The GFR TmPAH and ERPF/TmPAH ratios are, of course, much lower than in a pair of normal kidneys combined (table 1) Thus increase in tubular mass outstrips increase in effective renal plasma-flow This is already evident in a healthy kidney as early as three weeks after removal of its functioning mate (VAH 45848), in which the ERPF is only 61 8 per cent of normal but the TmPAH is 73 8 per cent of normal (table 1, fig 4) This case demonstrates that rate of restitution is in the following descending order TmPAH > ERPF > GFR The TmPAH of a healthy solitary kidney eventually exceeds that of two normal kidneys, the ERPF eventually approximates that of two normal kidneys, whereas the GFR is limited to well below that in a combined pair of normal kidneys

6 *Internal diameter of the renal artery* for the congenitally or the surgically solitary kidney is only about 12 5 per cent greater than that for a normal kidney (Maluf, '58) This difference is small but significant although the blood-flow through a single solitary kidney is almost twice that through a normal kidney Accommodation for doubling of blood-flow nevertheless exists in this slight increase in diameter, as may be calculated from the following derivation of Poiseuille's law $Q_s/Q_n \propto R_s^4/R_n^4$, in which Q_s and Q_n are the quantities of blood flowing through the artery of a solitary kidney and of a single kidney of a normal pair, respectively, and R_s^4 and R_n^4 are the radii, raised to the 4th power, of the

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* The volume of a glomerulus like that of a sphere varies directly with the cube power of the diameter and thus increases rapidly with relatively small increase in diameter

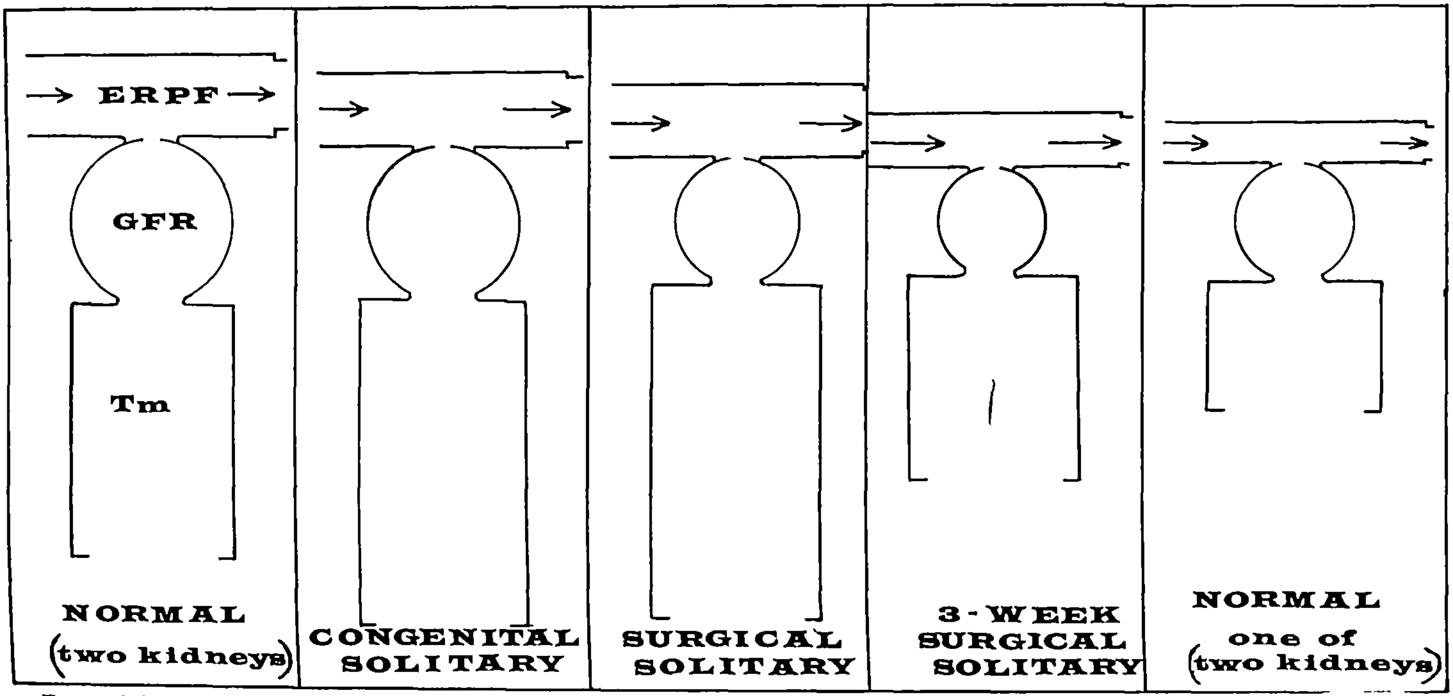

FIG 4 Schematic diagrams of normal and solitary human kidneys *ERPF*, effective renal plasma flow, *GFR*, glomerular filtration-rate, *Tm*, tubular maximum for para aminohippurate Areas of corresponding rectangles and circles indicate relative values of ERPF, GFR, and TmPAH in different kidneys Note that TmPAH of each type of solitary kidney exceeds TmPAH of two normal kidneys, that ERPF of solitary kidney approximates that of two normal kidneys, and that GFR falls short of two normal kidneys

artery of the solitary kidney and of a single kidney of a normal pair, respectively. For example, VAH 44070 has a renal artery 8.1 mm in internal diameter whereas a young man of same age and size with two normal kidneys has a renal artery 7.2 mm in internal diameter (Maluf, '58). Then $Q_s : Q_n \propto 4.1^4 : 3.6^4$, or 1.7, that is a difference of 85 per cent, which is almost the difference in actual effective renal plasma- or blood-flow (table 1).

DISCUSSION

1. *Incidence of congenital solitary kidney.* In discussing monstrosities, Aristotele remarked that "No animal, indeed, has ever been born without a heart, but they are born without a spleen or with two spleens or with one kidney . . . and all these phenomena have been seen in animals perfect and alive." Unilateral renal agenesis in domestic animals has been well documented (Hunt, '18; Tannreuther, '23; Mack, '49; Bloom, '54 and others). Its infrequency indicates the large number of animals Aristotele must have dissected. Incidence of congenital kidney in man was 1 : 1,817 in an aggregate of 92,690 necropsies (Anders, '10) and 1 : 1,444 in 13,000 necropsies at Bellevue Hospital (Campbell, '28). While the senior author was in charge of the urological service of the Houston V. A. Hospital, all of the 2,000 new admissions to that service had at least preliminary evaluation of their "upper tracts" by intravenous and/or retrograde pyelography. Among these were 4 patients with congenital solitary kidney (VAH 50940, 47737, 44070, 53860) confirmed by aortography and cystoscopy. The unexpectedly high incidence of 1 : 500 cannot be explained by a practical absence of female patients from the V. A. Hospital because this abnormality is not sex-linked although it has been reported somewhat more frequently for men (Ballowitz, 1895; Moore, 1899; Gérard, '05b; Anders, '10; Fortune, '27; Collins, '32). The moderately higher incidence in males in the above necropsies may be because more males than females were necropsied (Ballowitz; Anders).

2. *Previous physiological measurements on human solitary kidneys.* Urea-clearance* during diuresis is somewhat less in the acquired solitary kidney than in two normal kidneys (Foster, '25). Ellis and Weiss ('33) found normal phenosulfonphthalein (PSP) excretion and blood urea-concentration in two young adults with surgically solitary kidneys, the urea-clearance was only 70 per cent of normal and the creatinine-clearance was within lower limit of normal. These data suggest tubular hypertrophy (PSP) and lack of equivalent rise in GFR (urea-clearance). Welsh et al. ('44) presented 2 cases of surgically solitary kidney. The first was complicated by eclampsia, the second showed high TmDiodrast, indicating tubular hypertrophy. Michie et al. ('54) found the GFR/TmPAH and ERPF/TmPAH ratios less than normal in hypertrophied, surgically solitary kidneys. They found the FF elevated and postulated that ERPF in such kidneys falls short of GFR because the kidney is enclosed in a fibrous capsule which may not expand commensurately with renal hypertrophy, thus producing a presumed rise in intrarenal pressure which might depress renal blood-flow. This theory is

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*The concept of clearance had not been introduced when Foster wrote. He used the Addis excretion-ratio for urea, which is strictly a clearance formula and represents the virtual volume of blood cleared of urea per hour instead of per minute.

not supported by our findings of diminished FF in both surgically and congenitally solitary kidneys and of almost complete restitution of the original total effective renal blood-flow in the acquired solitary kidney In the congenitally solitary kidney, deposition of renal capsule in embryonic development would occur probably in accordance with renal growth

3 Physiological measurements on the solitary kidney of animals Rosenstein (1871) and Sacerdotti (1896) noted that the unilaterally nephrectomized dog excretes as much urea on the first and subsequent postoperative days as preoperatively Sacerdotti wrote "I was astounded at this result " The blood urea-concentration of these dogs, however, must have been elevated because of inevitable fall in urea-clearance resulting from nephrectomy Unilateral nephrectomy in rats, rabbits, and dogs results in permanent drop in urea-clearance, studied under urea-loading (Addis et al '24, MacKay, '32 a and b) After unilateral nephrectomy in the rat, the GFR and TmDiodrast recover maximally to about 80 per cent of normal (Braun-Menendez and Chiodi, '47) Hinman's ('26) data indicate that urea-clearance in the dog, without urea-loading, is fully regained by four weeks after unilateral nephrectomy but that maximal PSP excretion recovers earlier This indicates faster recovery of Tm than of GFR, as in man Dogs may recover initial GFR, ERPF, and TmPAH four to five months after unilateral nephrectomy (Maluf, '49)

4 Compensatory enlargement of the acquired solitary kidney At the age of 8 or 9 months the human fetus has its full quota of glomeruli (Eckhardt, 1888, Külz, 1899, Herring, '00, Stoerck, '04) Each of a pair of normal human kidneys has about 1 × 10^6 glomeruli, ranging between 6 × 10^5 and 1 2 × 10^6 (Kittelson, '17, Vimtrup, '28, Moore, '31) Simon's (1870, 1871) removal of a sound kidney to cure a ureterocutaneous fistula aroused curiosity as to how an organism lives with one kidney Studies on unilaterally nephrectomized animals (rats, rabbits, dogs) indicate that enlargement of the remaining kidney is the result of 1) increase in size but not in number of the glomeruli, 2) increase in size of the tubules by cell-enlargement (hypertrophy*) and cell-division (hyperplasia*), and 3) dilatation of the blood-vessels (Rosenstein, 1871, Gudden, 1876, Grawitz and Israel, 1879, Ribbert, 1882, Golgi, 1883, Lorenz, 1886, Albarran, 1899, Galeotti and Villa-Santa, '02, Arataki, '26b, Saphir, '27, Jackson and Shiels, '27, Moore, '29, Bollman and Mann, '35, Allen, '35, Allen and Mann, '35) There is no addition of new glomeruli beyond the normal quota of one adult kidney even in rats which had undergone unilateral nephrectomy when only one to several days old, before formation and differentiation of all glomerular fundaments (Arataki, '26a and b, Kittelson, '17, Jackson, '27, Moore, '29) Most of the compensatory enlargement occurs in the convoluted segments and is thus mainly cortical rather than medullary (Oliver, '24) In rats, tubular enlargement is especially prominent in the proximal segment (Oliver, '39, '45) This accords with our finding that Tm increases remarkably whereas GFR does not attain normal (table 1 fig 4) Compensatory enlargement of the pronephros of embryonic amphibians, after extirpation of the opposite pronephros, occurs by cell-division and cell-enlargement and not by addition of new nephrons (Howland, '21, Fox '56) Dogs and rabbits, like rats, are born with an incomplete number of glomeruli (Galeotti and Villa-Santa) The data of these investigators suggest that unilateral nephrectomy in such young rabbits results in enlarged contralateral kidneys with the normal number of glomeruli (their table 1) The data on their one young dog indicates that additional glomeruli developed in the remaining kidney Glomerular counts from only nine meridional sections, 6μ thick, of a kidney are, however, unreliable (see, for instance, Kunkel, '30)

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* *Hypertrophy* is "an increase in size of an organ, independent of natural growth, due to enlargement or multiplication of its constituent cells " *Hyperplasia* (introduced by Virchow, 1854, in his *Handb der spec Path u Ther* I, pp 327–28) is "an increase in the size of a tissue organ owing to an increase in the number of cells," it is synonymous with "numerical hypertrophy " These definitions given in the *New Gould Medical Dictionary* for 1953 (Blakiston Co , Phila) are those of Virchow (1871)

Is intrarenal vascular and lymphatic dilatation a prominent component of compensatory renal enlargement? Rosenstein (1871) noted tubular hypertrophy but denied consistent increase in size of glomeruli in the enlarged, surgically solitary kidney of dogs and rabbits He believed that the bulk of renal enlargement is due to engorgement with blood and lymph Morel and Verliac ('13) found near-maximal weight-gain (32 to 37 per cent) of the kidney of rats as early as the forth to tenth day after unilateral nephrectomy They considered it inconceivable that this could be due to hyperplasia but presented no microscopic studies Carnot ('13) found renal weight-gain of 47 per cent by the seventh day after unilateral nephrectomy in rats He spoke of this as "hyperplasie compensatrice" but had no microscopic data Maximal rate of renal weight-gain a few days after unilateral nephrectomy was noted in young rats by Levin et al ('56) although this gain was about a third of that reported by Morel Verliac and Carnot Levin et al worked with young rats in which mitosis in the renal tubules is normally evident They reported no increase in rate of mitosis in the kidney undergoing compensatory hypertrophy Albarran (1899) noted that as early as 24 hours after unilateral nephrectomy the remaining kidney is congested and that mitotic cells are evident in its tubules Jackson and Shiels ('27) found no evidence of vascular congestion or edema in the kidney of albino rats as late as 7 days after unilateral nephrectomy The remaining kidney continued to enlarge for several weeks, which appears concomitant with increase of TmDiodrast (Braun-Menendez and Chiodi, '47) Allen et al ('35) saw vascular engorgement in the murine solitary kidney

Most authors agree that when a functioning kidney is removed from man the ensuing enlargement of the remaining kidney is due to 1) dilatation of blood-vessels, 2) enlargement of the glomeruli 3) mitosis of tubule-cells (hyperplasia), and 4) enlargement of the tubule cells (hypertrophy, strictly) (Perl, 1872, Eppinger, 1879, Albarran, 1879 Leichtenstern 1881 Lorenz, 1886, Eckhardt, 1888)

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[5] *The congenitally solitary kidney* has approximately the same number of nephrons as a normal kidney (Boycott '11, for rabbit, Moore, '30a, for man) The glomeruli and tubular epithelium are enlarged, as also noted by Beckmann (1856), Beumer (1878), Leichtenstern (1881), Guttmann (1883) Eckhardt (1888) Gladstone ('15), and others The congenital hypoplastic kidney has a

subnormal number of nephrons (Moore, '30a), on the other hand, the enlarged kidney of corporeal hemihypertrophy has a normal number of nephrons (Moore, '30b) Glomerular counts (Boycott, Moore) indicate that the congenitally solitary kidney is not two fused kidneys but one hypertrophied kidney Developmental block and regression of a metanephric fundament appears to be due, typically, to retardation in development of the corresponding mesonephric (wolffian) duct Thus a) In Boyden's ('32) human embryo with presumptive left renal agenesis, the right metanephric fundament was normal but the left such fundament was rudimentary, showing no tubules, and the left mesonephric duct was blocked and dilated proximally, b) tubules failed to form in metanephric fundaments into which the ureter had not entered, in a strain of mice with inherited renal defects (Brown, '31), c) 75 per cent of human cases with unilateral renal agenesis show absence of corresponding ureter (Collins '32), d) in spite of experimental extirpation of the ureter (wolffian duct) in chick embryos, the metanephric fundament appears but does not differentiate (Boyden) Primary defect in formation of metanephric fundament, however, may occur as indicated by a patent ureter on the involved side in about 10 per cent of human cases of renal agenesis (Fortune, '27) The wall of the ureter of a healthy solitary kidney is thicker than normal (cf Gérard, '05a, Ballowitz, 1895, Moore, 1899, and others) The same is true for the pronephric duct of amphibian embryos which had undergone contralateral pronephrectomy (Howland)

It is noteworthy that when unilateral nephrectomy is done even when new glomeruli are still forming, as during the first several postnatal days of albino rats (Kittelson, '17, Arataki, '26a), the definitive number of glomeruli in the remaining kidney are not increased (Arataki, '26b, Moore, '29) The same applies to unilateral pronephrectomy in amphibian embryos (Howland, Fox) These data fit in with the fact that the congenitally solitary kidney has the same number of nephrons as a normal kidney

There is no rigorous evidence that the congenitally solitary kidney has an added quota of nephrons Falk (1881) and Palma (1891) noted "no evidence of enlargement of glomeruli or renal tubules" in their 2 cases of congenitally solitary kidney Their brief papers are almost exempt from adequate data Falk's case was a 34-year-old man killed by violence His solitary left kidney was only 12 by 9 by 2 cm The man had been apparently healthy but there is no statement as to his weight Palma's case was a 45-year-old man who had died from oral cancer His solitary kidney was 13 5 by 7 by 4 cm Beumer (1878) made careful measurements in a 31-year-old man who died from a fall and who had been healthy His solitary kidney was 15 by 7 5 by 4 cm The averages of his measurements of diameter of glomeruli and of the proximal and distal convoluted segments of the tubule are distinctly above those of his two normals He indicated no attempt at measuring the glomeruli only at their greatest diameter and emphasized the spuriously wide variation in his glomerular measurements, thus attempting to invalidate differences between solitary and normal kidneys

6 *Factors in compensatory renal enlargement a) Potentiating factors i) Accumulation of "urinary products* " Sacerdotti (1896) removed half the blood from small,

healthy, unoperated dogs twice daily replacing this with an equal quantity of blood from bilaterally nephrectomized large dogs Daily excretion of urea rose and the kidneys showed no evidence of damage (no albuminuria, erythrocytes, or casts) After several days of this the renal tubules showed cells in mitosis A diet containing a large quantity of urea augments compensatory renal enlargement in unilaterally nephrectomized rats (Allen, '35) Bollman and Mann ('35) indicated that compensatory hypertrophy of the remaining canine kidney is increased by transplantation of its ureter to the duodenum or jejunum, urinary products accumulate and survival is 15 to 20 days

ii) *Diet* Compensatory renal enlargement is augmented in rats by diets high in protein or free amino acids (Wilson, '33, Allen and Mann, '35, Chanutin, '34, Chanutin and Ludwig, '39, Allen and Mann, '35, Oliver, '45)

iii) *Steroids* Welch et al ('42) reviewed the effect of steroids on renal size Lattimer ('42) and Welch et al found that testosterone raises the TmDiodrast and GFR in dogs

b *Inhibiting factors* i) *Partial constriction of the renal artery* prevents compensatory renal enlargement in rats (Block et al , '53)

ii) *Starvation* inhibits compensatory renal enlargement in rats and dogs (Sacerdotti, 1896, Block et al , '53)

iii) *Hypophysectomy* inhibits compensatory renal enlargement in rats (McQueen-Williams, '40, Rolf and White, '53) and amphibians (Gonzalez, '38) The portion of the hypophysis which is responsible is the anterior or glandular component (Winternitz and Walters, '40, White et al , '42), of this the eosinophil cells appear to be important (Barnett et al , '43) Thus, urea-clearance appears to be elevated in acromegalic persons whereas in Cushing's disease (basophilic adenoma) the ERPF, GFR, and TmDiodrast were normal (based on one case) Braun-Menendez ('49) confirms that hypophysectomy prevents compensatory renal enlargement in rats but remarks "Most authors have overlooked the marked renal atrophy which follows hypophysectomy and their results have been negative because their controls were wrong"

c *Noncontributory factors* Gestation, forced exercise, adrenocortical extract, and osmotic diuresis do not effect compensatory renal enlargement in rats (Allen and Mann, '35)

SUMMARY

This is a study of renal dynamics in two young men with healthy, congenitally solitary kidneys, in one young man with unilateral congenital renal hypoplasia and contralateral renal enlargement, and in seven men with surgically solitary kidneys This is the first such study of the congenitally solitary kidney so far as we know

Renal dynamics of both the congenitally and surgically solitary kidneys are essentially equal This reinforces previous anatomical studies that both the congenital and acquired solitary kidneys are structurally identical Previous workers have shown that the number of nephrons in a hypertrophied solitary kidney is essentially the same as in a single kidney of a normal pair

The TmPAH of the healthy solitary kidney actually exceeds that of two normal kidneys

The ERPF of the healthy solitary kidney approximates that of two normal kidneys

The GFR of the healthy solitary kidney falls short of that of two normal kidneys

The internal diameter of the renal artery of a healthy solitary kidney is slightly (about 12 5 per cent) but significantly greater than that of a normal kidney Since volume-flow of a liquid through a tube varies with the fourth power of the radius of the tube, other things being equal, this small increase in arterial caliber is enough to allow for the doubling in volume-flow of blood which exists in the artery of a healthy solitary kidney

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PERSISTENT LUMBAR SINUS DUE TO FOREIGN BODY

ROBERT W McKAY AND LAWRENCE K BOGGS*

From Charlotte Memorial Hospital, Charlotte, N C

We occasionally observe the use of suture material in kidney surgery that is not absorbable The following case we believe illustrates this principle It is a well known and widely accepted principle of urologic surgery that absorbable suture material is to be used during any operative procedure whenever the urinary tract is opened Recently we observed an interesting complication subsequent to a violation of this principle

CASE REPORT

J S , Charlotte Memorial Hospital No 186437, a 28-year-old white married woman, was admitted to Charlotte Memorial Hospital on June 5, 1956 for investigation of a draining sinus in the right flank According to the patient's statement, 8 months prior to this admission she had had a stone removed from her right kidney and she was told that in conjunction with this operation a string was tied around her kidney and hooked to a rib

Postoperatively, drainage was intermittent The wound would heal, only to break down and drain a moderate amount of purulent material She elected to come to Charlotte Memorial Hospital Physical examination was unremarkable except for a small opening in the middle of the right lumbar scar which exuded pus on pressure Laboratory reports included a normal hemogram, urinalysis (a few pus cells per high power field), a normal blood urea nitrogen and a negative VDRL Intravenous pyelography demonstrated prompt function bilaterally, with a malrotation of the right kidney assumed to be postoperative change Retrograde studies verified this and showed a dilated, tortuous ureter on the right All films showed clearly two notches in the eleventh rib (fig 1) and in no film was any extravasation of dye outside the urinary tract noted Culture and sensitivity studies of the drainage grew B pyocyaneus which was insensitive to all antibiotics tested including furadantin and chloromycetin

The wound was explored At operation a probe could be easily passed from the ostium of the sinus cephalad to the border of the eleventh rib Following the injection of the sinus tract with methylene blue, the roof of the tract was incised and in the tract lay a large silk suture This was followed into the depths of the sinus and was found to be looped around two notches on the eleventh rib The sinus tract was dissected out in its entirety The rib with the osteomyelitis portion was resected and the wound packed with iodoform gauze The wound drained for a few days but closed nicely She was given albamycin 250 mg t i d and the wound irrigated with polymyxin

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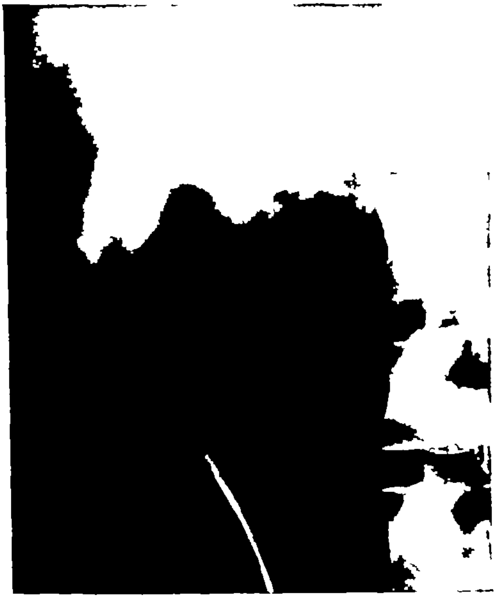

FIG 1 Note notching in eleventh rib caused by silk suture

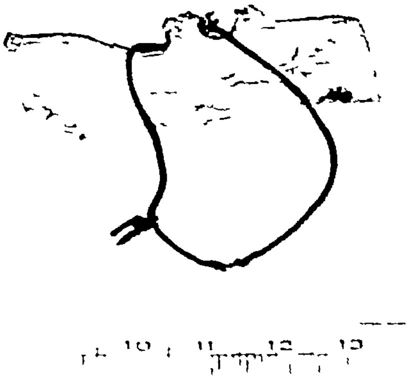

FIG 2 Resected portion of rib with suture fitting in area of osteomyelitis

DISCUSSION

Silk or cotton as a suture material certainly has no place below the skin in urologic or any other surgery that necessitates drainage from a potentially infected field Suture material will act as a foreign body nidus and will be the source and/or cause of continuous drainage until removed surgically or extruded spontaneously When first seen it was thought that the drainage was urine instead of pus To what structure the large silk suture was previously attached beside the rib we can only surmise The patient was told that it was around the

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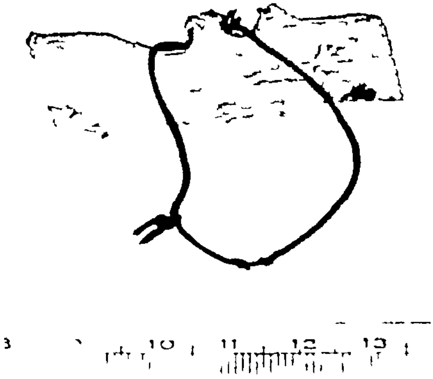

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SUMMARY

In the case just reported, apparently a large silk suture was used to perform a nephropexy following a pyelolithotomy by anchoring the kidney to the eleventh rib The results were notching of the rib and osteomyelitis that caused a persistent sinus which was infected with B pyocyaneus The silk suture acted as a foreign body Treatment was dissection of the sinus tract, resection of the affected portion of the rib, removal of the silk suture and postoperative antibiotic orally and by irrigation of the sinus tract

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URETERAL ATRESIA PRODUCING GIANT HYDROURETER

GREGORY S SLATER

Your attention is called to the presence of a large abdominal mass, discovered in a 5-month-old infant, which proved to represent a giant hydroureter

A 5-month-old white, robust, active male infant was examined 2 weeks prior to his admission to the hospital and found to have an oblong mass in a transverse position just above the left iliac crest that was palpated as approximately 3 inches in length and 1 inch in diameter, it was firm and slightly movable The pediatrician (Dr Harold Greenblatt) who made this initial examination believed that it represented a fecal mass in the sigmoid However, as enemas did not resolve the mass the baby was admitted to the hospital for study

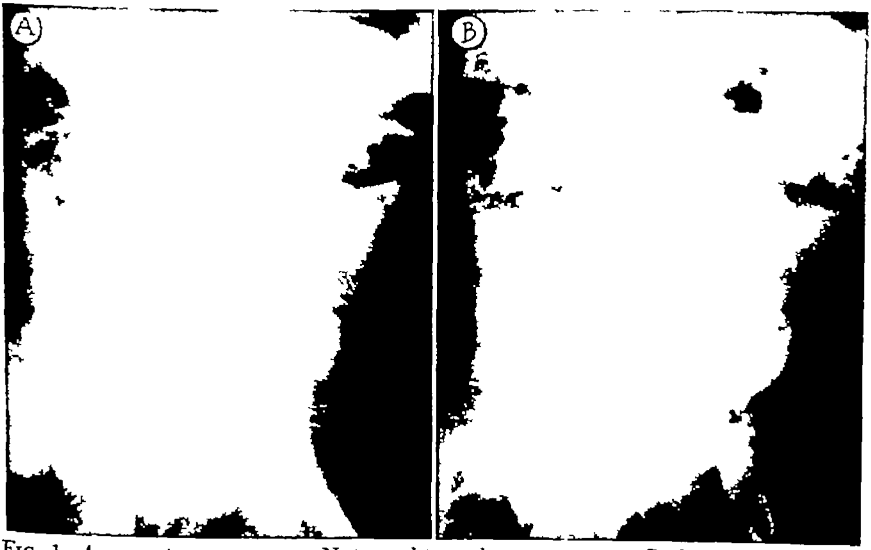

FIG 1 A, excretory urogram Note right pyeloureterogram Catheter in bladder B, cystogram shows compression of bladder to right by extrinsic mass Faint right pyeloureterogram also seen

Physical examination was entirely negative except for the abdominal mass

Laboratory studies revealed a normal hemogram negative urinalysis, and a normal chest x-ray An excretory urogram (fig 1, A) showed a normal functioning right kidney and ureter No left kidney was visualized A careful search failed to show any evidence of an ectopic kidney Cystography (fig 1, B) disclosed an extrinsic mass compressing the bladder to the right In the belief that a cystoscopy and retrograde study would be of help, this was attempted on two occasions the first time, using the Butterfield infant cystoscope F15, and the second time, using the McCarthy infant cystoscope F11 Despite a meatotomy, an instrument could not be passed through the prostatic urethra due to the sharp angulation in this area At this juncture, it was the opinion that we were dealing

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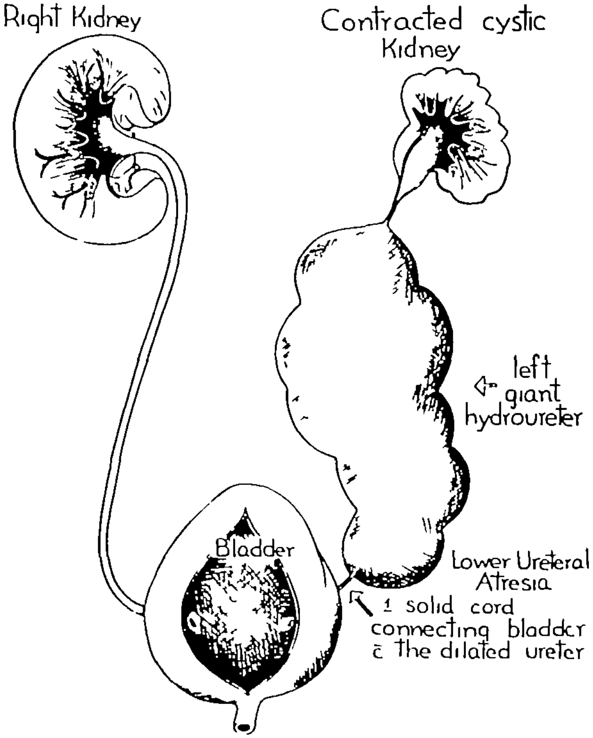


FIG 2 Diagram shows pathological process prior to surgery and its relationship to entire urinary tract

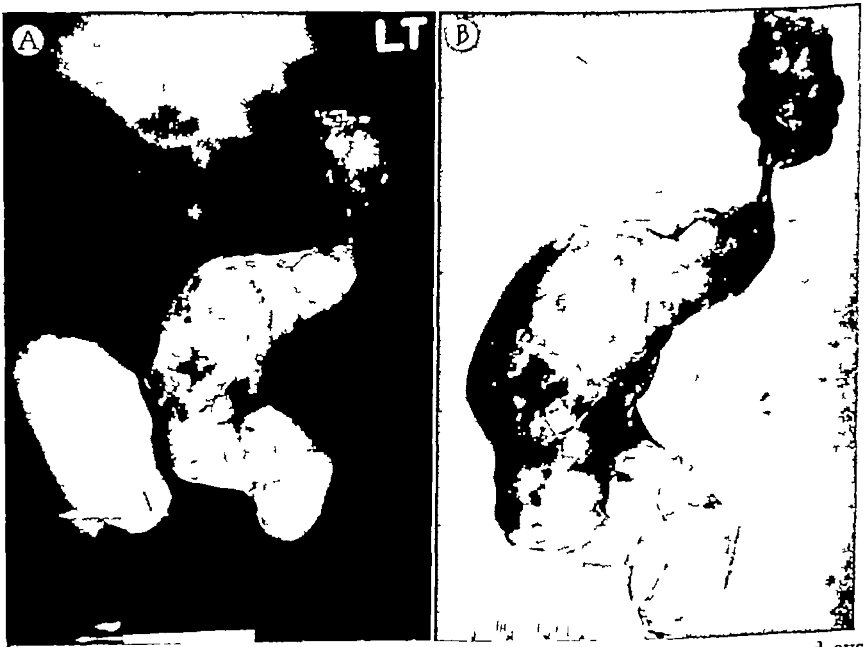


FIG 3 Gross specimen *A*, superimposed on x-ray film (pyeloureterogram and cystogram) *B*, left kidney and dilated ureter

with a Wilms' tumor in an ectopic (or nephroptotic) left kidney An exploratory operation was planned

Operation A left lower quadrant transverse incision was made, giving access to the left retroperitoneum as well as the intraperitoneal contents Through this incision, it was soon apparent that the tumor which had been palpated preoperatively, was a large, firm, smooth surface retroperitoneal cystic mass measuring 8–10 inches by 2½ inches The peritoneum was adherent to the wall of this mass and was dissected from it with difficulty Further exploration disclosed the true nature of this lesion (figs 2 and 3) It was found to be attached to the bladder distally by a 2 inch solid fibrous cord Cephalad, it narrowed to a small patent tube, which in turn was attached to a small atrophic cystic renal mass

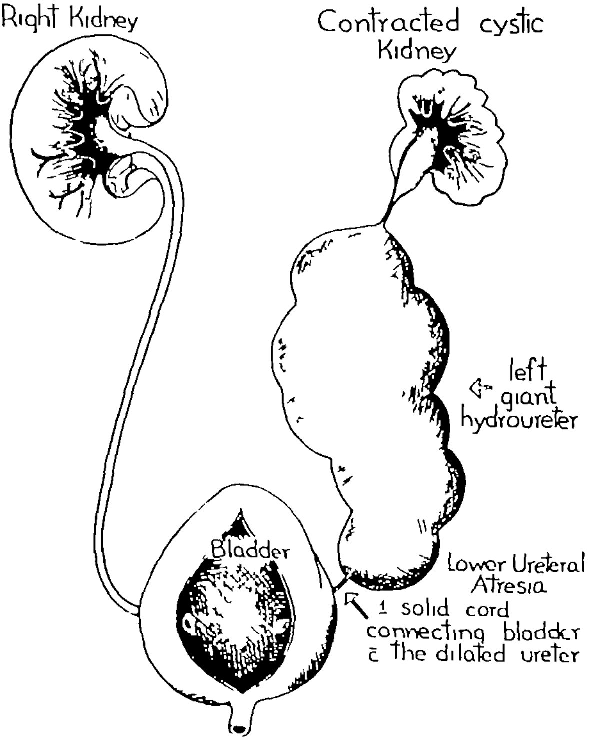
DISCUSSION

The ureter is derived from the lower end of the mesonephric duct as a tiny budlike outgrowth This occurs at the fifth week of fetal development Later in fetal growth, the kidney ascends and the former budlike outgrowth, attached to the renal mass, forms the renal pelvis and ureter It is felt that in this instance the early budlike outgrowth (metanephric diverticulum) never became patent at its origin, that the functioning kidney excreted urine into the blind-ending ureter and caused the giant hydroureter found at surgery Subsequently, this process also produced a secondary, atrophic, nonfunctioning left kidney

SUMMARY

A case of ureteral atresia producing a giant hydroureter in a 5-month-old infant is presented Aside from being unusual this case serves as a reminder that abdominal masses in children very often arise from urinary tract disease

73 Cedar St, New Britain, Conn



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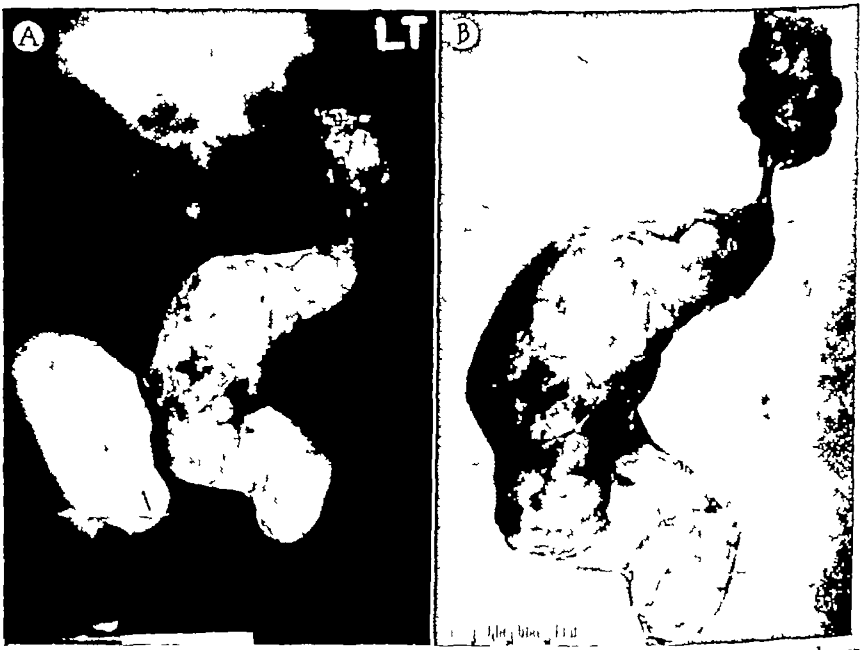

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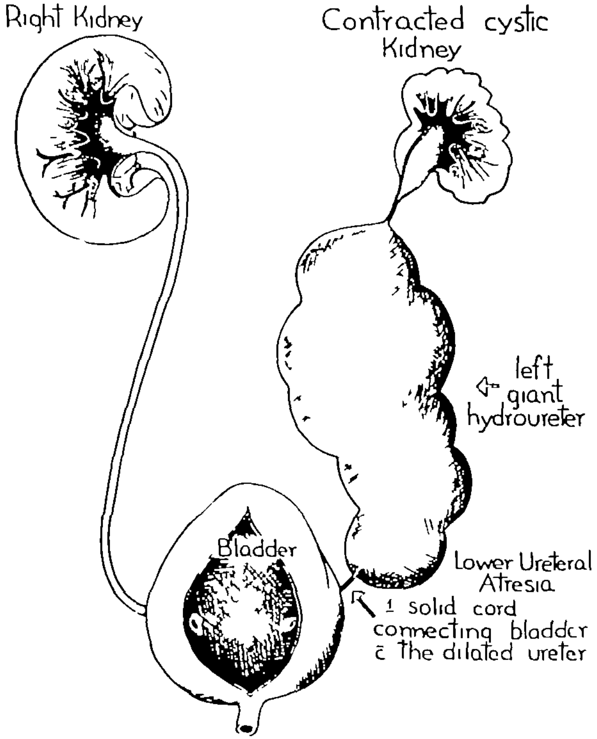

FIG 2 Diagram shows pathological process prior to surgery and its relationship to entire urinary tract

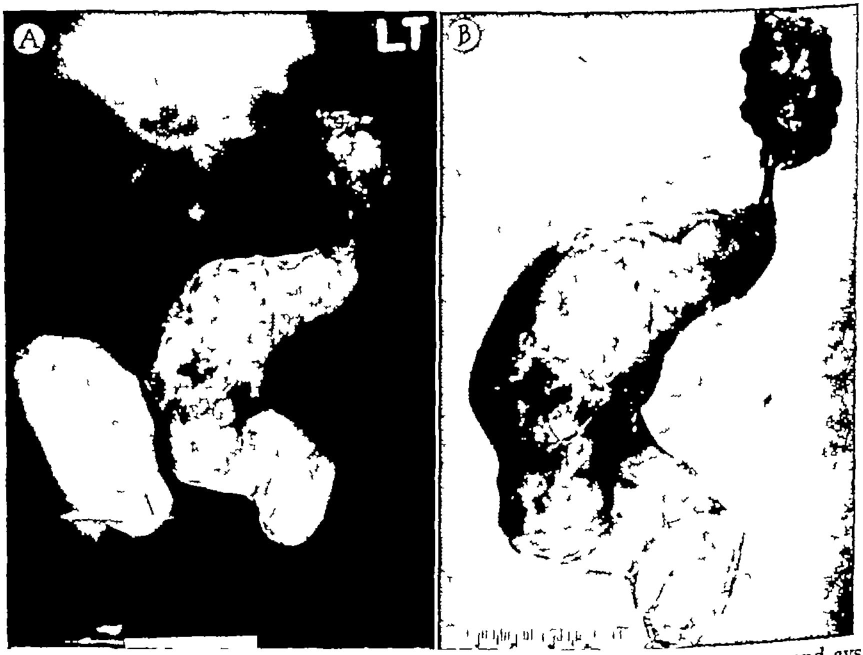

FIG 3 Gross specimen A, superimposed on x-ray film (pyeloureterogram and cystogram) B, left kidney and dilated ureter

with a Wilms' tumor in an ectopic (or nephroptotic) left kidney An exploratory operation was planned

Operation A left lower quadrant transverse incision was made, giving access to the left retroperitoneum as well as the intraperitoneal contents Through this incision, it was soon apparent that the tumor which had been palpated preoperatively, was a large, firm, smooth surface retroperitoneal cystic mass measuring 8–10 inches by 2½ inches The peritoneum was adherent to the wall of this mass and was dissected from it with difficulty Further exploration disclosed the true nature of this lesion (figs 2 and 3) It was found to be attached to the bladder distally by a 2 inch solid fibrous cord Cephalad, it narrowed to a small patent tube, which in turn was attached to a small atrophic cystic renal mass

DISCUSSION

The ureter is derived from the lower end of the mesonephric duct as a tiny budlike outgrowth This occurs at the fifth week of fetal development Later in fetal growth, the kidney ascends and the former budlike outgrowth, attached to the renal mass, forms the renal pelvis and ureter It is felt that in this instance the early budlike outgrowth (metanephric diverticulum) never became patent at its origin, that the functioning kidney excreted urine into the blind-ending ureter and caused the giant hydroureter found at surgery Subsequently, this process also produced a secondary, atrophic, nonfunctioning left kidney

SUMMARY

A case of ureteral atresia producing a giant hydroureter in a 5-month-old infant is presented Aside from being unusual this case serves as a reminder that abdominal masses in children very often arise from urinary tract disease

73 Cedar St , New Britain, Conn

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URETERAL REGENERATION VI DELAYED URINARY FLOW IN THE HEALING OF UNSPLINTED URETERAL DEFECTS

FRANK HINMAN, JR AND RUDOLF OPPENHEIMER

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The details of the healing processes in experimental ureteral defects are gradually being uncovered Fibrous closure of the defect is dominant in repair, but new smooth muscle is formed to restore normal architecture to the ureteral wall[1] [2] Urine flow delays healing and markedly increases the fibrous reaction of the surrounding connective tissue[3] Finally, apposition of the ureteral defect to the unyielding psoas fascia prevents early closure and so promotes grossly ab normal healing[4]

Inadequate primary epithelization is the factor uniformly associated with defective healing in these various experiments If new epithelium cannot be laid down immediately in tubular form, abnormal smooth muscle is formed, so that repair is either incomplete (fistula, double lumina), or imperfect (sacculations, strictures, massive fibrosis, bone formation)

Since urinary flow through the fresh defect, with consequent local extravasation, adversely affected healing, we wished to determine if temporary urinary diversion would modify this delaying effect Such "diversion" is accomplished experimentally by temporary proximal ureteral obstruction, since actual diversion by ureterostomy or nephrostomy in the dog introduces infection Diversion might reduce local tissue reaction, as epithelization should be complete and the area watertight before release of the obstruction

Experiments were also designed to compare these "temporary" cases with defects allowed to heal after permanent proximal obstruction of the ureter Johanson[5] has shown for the urethra, that contraction and stricture are reduced if urinary flow is permitted during healing He feels this to be an hydraulic action The urethra and ureter, however, are structurally quite different but hydraulic effects could play a role in ureteral repair Experiments were made to test this possibility

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Supported by the Christine Breon Fund for Medical Research

Read at annual meeting, American College of Surgeons, San Francisco, October 8–12, 1956

[1] Oppenheimer, Rudolf and Hinman, Frank Jr Ureteral regeneration I Contracture vs hyperplasia of smooth muscle J Urol , **74** 476–484, 1955

[2] Hinman, Frank Jr and Oppenheimer, Rudolf Smooth muscle regeneration in repair of experimental ureteral defects II The significance of the double lumen J Urol , **75** 428–432, 1956

[3] Oppenheimer, Rudolf and Hinman, Frank Jr Ureteral regeneration III Effect of urinary flow in the absence of splint Surg , Gynec & Obst , **103** 416–422, 1956

[4] Hinman, Frank Jr and Oppenheimer, Rudolf Ureteral regeneration IV Fascial covering compared with fatty connective tissue J Urol , **76** 729–735, 1956

[5] Johanson, Bengt Reconstruction of the male urethra in strictures (Application of the buried intact epithelium technic) Act Chir Scan , Suppl 176, 1953

EXPERIMENTAL PROCEDURES

Nineteen mongrel dogs were subjected to a muscle-splitting, extraperitoneal exposure of the upper third of the right ureter by a technique previously described [3] In 15 animals, a defect was created by excising 50 per cent of the circumference of the ureter for a distance of 1 5 cm, in partial imitation of the defect found after simple longitudinal incision of a ureteral stricture (such as would clinically be treated by intubated ureterotomy) In all instances, a loop of polyethylene tubing was placed proximally to occlude the ureter (fig 1) for one week To simplify release of the obstruction, a method was devised (fig 1, A) which allowed release of the wire holding the tubing through a simple subcutaneous incision

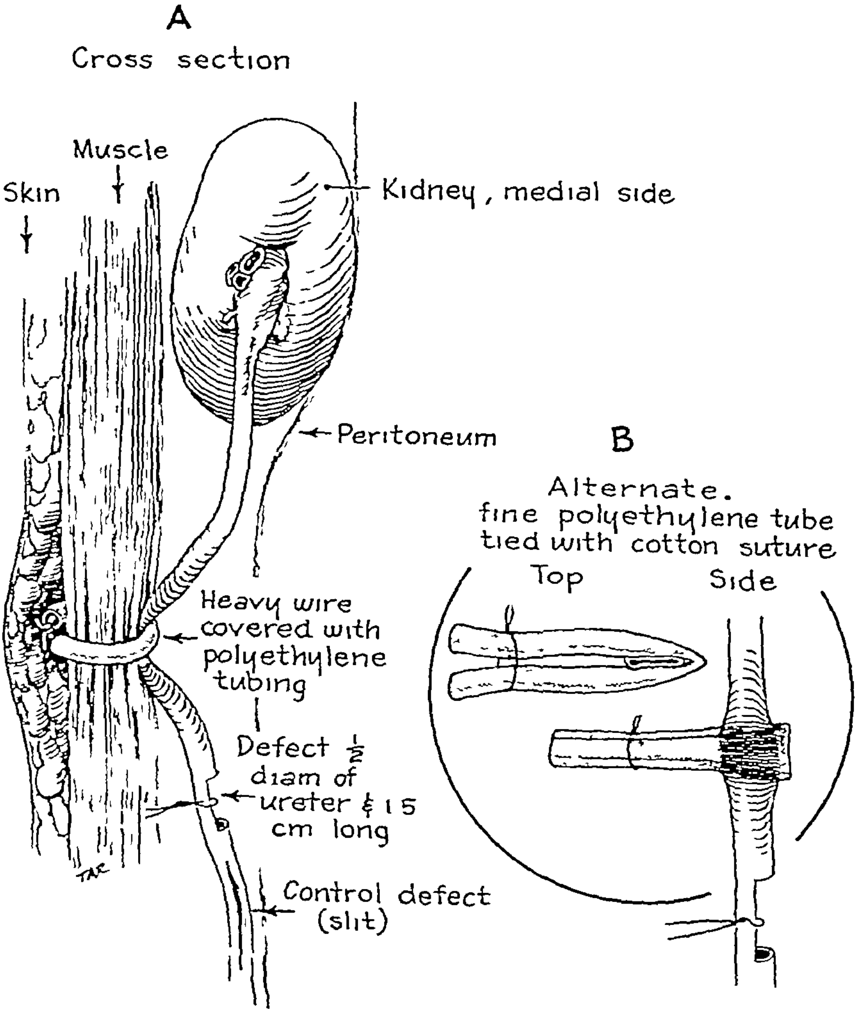
A
Cross section
Muscle
Skin
Kidney, medial side
Peritoneum
Heavy wire covered with polyethylene tubing
Defect ½ diam of ureter & 1 5 cm long
Control defect (slit)
TAF
B
Alternate.
fine polyethylene tube tied with cotton suture
Top
Side

Fig 1 Diagram of experimental procedure A, with external wire B, with internal loop

In other animals, for comparison, polyethylene tubing was tied in a simple loop about the ureter (fig 1, *B*), this however requires a transabdominal incision for release No drains were used In 7 instances the compressed ureter was not damaged, while in 8 cases the ureter became occluded permanently Those animals with permanently occluded ureters served as controls

The constricting band in 12 animals was released after one week In 3 animals the obstruction was left 3 to 4 times longer to try to compare the effects of long continued "diversion", but this comparison was abandoned when permanent obstruction resulted in each instance

Results The animals were autopsied after varying periods and placed in 2 groups those with continued urinary flow (series A) and those with complete obstruction (series B) Those with continued flow then are the experimental

TABLE 1 *Temporary ureteral obstruction*

Dog No	Duration	Mucosal Regeneration (0 to 4+)	% Regeneration Smooth Muscle
	weeks		
68	3	±	0
192	4	±	0
288	4	3+	0
241	4	3+	20
132	6	4+	40
59	8	4+	100

(No 114 was miscut)

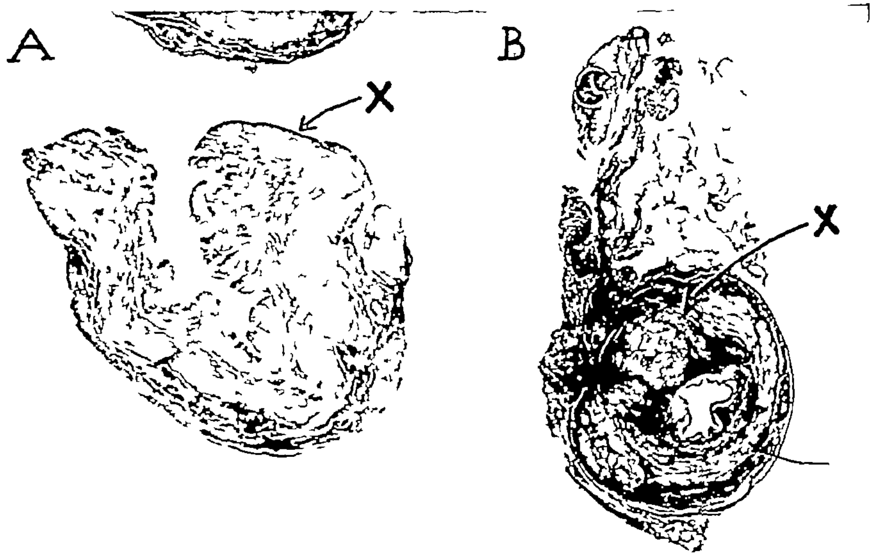

FIG 2 A, dog 192, 4 weeks after temporary urinary diversion Lumen lies open, with mucosa growing out (X) over granulation tissue (All photomicrographs X 20)
B dog 59, 8 weeks after temporary diversion Normal lumen surrounded by the original smooth muscle and an appreciable segment of new muscle (X)

series, and those obstructed make up a control group A third group (series C), which also serves as a control, is made up of those animals in which the urinary flow was not obstructed at all and in addition the ureter was fastened open against the peritoneum

Series A When the flow of urine through the experimental defect is prevented for 7 (or 8) days (table 1), ureteral regeneration at first is slow Complete epithelization (contrary to the observations on splinted defects by other workers)

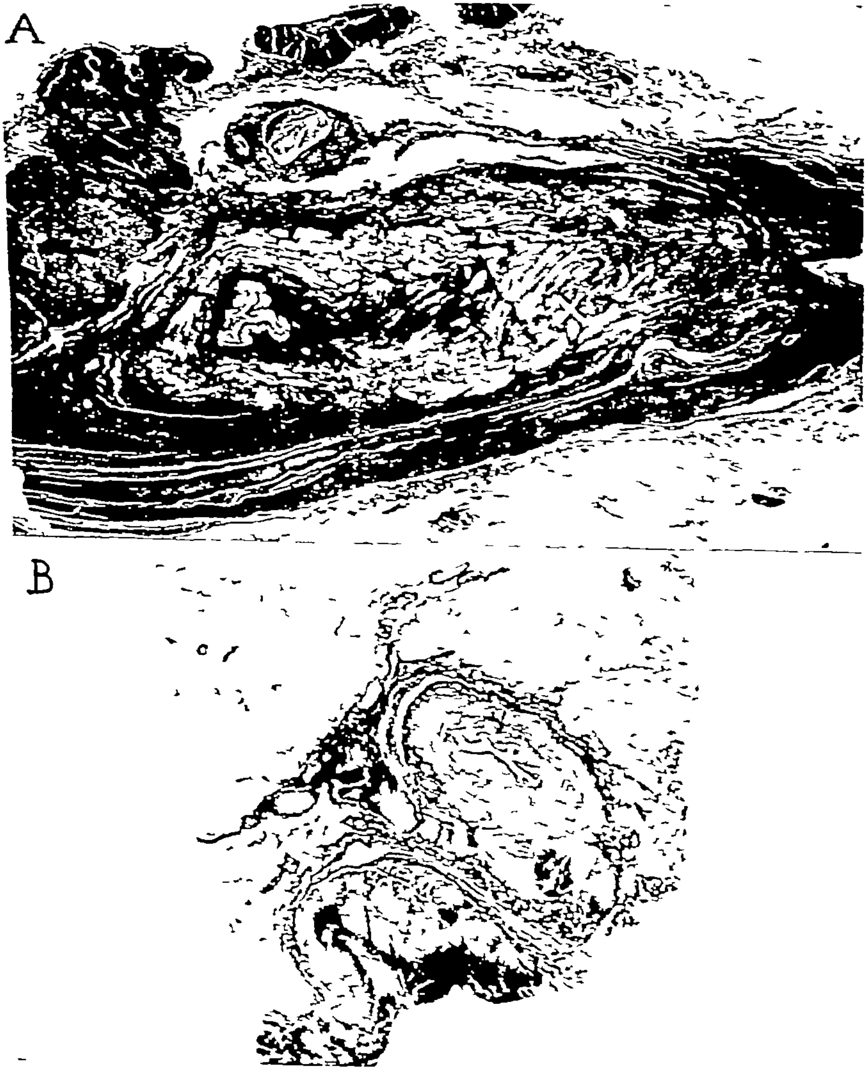

Fig 3 *A* dog 107 7 weeks after permanent diversion Unusually marked smooth muscle overgrowth (X)

B dog 117 4 weeks after permanent diversion Normal epithelization with almost complete regeneration of smooth muscle may not occur for 3 or 4 weeks Once the epithelial lining has been laid down, however, regrowth of muscle is reasonably orderly

The ureter after 4 weeks of regeneration (fig 2, *A*), has an open lumen with

TABLE 2 *Permanent ureteral obstruction*

Dog No	Duration	Mucosal Regeneration (0 to 4+)	% Regeneration, Smooth Muscle
	weeks		
117	4	3+	95
172	4	3+	0
107	7	4+	100
41	7	4+	95
79	8	3+	95
116	9	4+	20
185	12	4+	95

(No 156 omitted, damaged in experiment)

TABLE 3 *Free urinary flow*

Dog No	Duration	% Regeneration Smooth Muscle	Fibrous Reaction (0 to 4+)
	weeks		
31	6	70	4+
173	8	50	4+
152	9	20	3+
132	12	20	3+

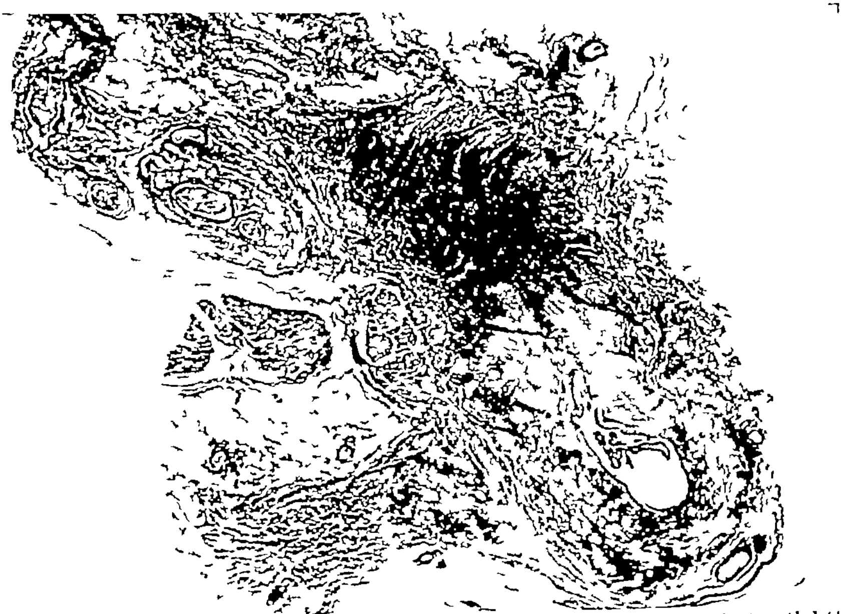

FIG 4 Dog 152, after 9 weeks of free urinary flow Dense scar at site of defect with little muscle regeneration

the mucosa growing around the margins No visible attempt at muscle growth has been made, ostensibly because epithelization is delayed After 8 weeks (fig 2, *B*), the lumen is reconstituted neatly and new muscle can clearly be seen bridging the defect

Series B Absence of urinary flow through the defect (table 2) favorably affects the pattern of healing Mucosal regeneration goes ahead more evenly and rapidly, so that after 4 weeks it was virtually complete Similarly, even in these early specimens, muscle regeneration is progressing rapidly, with little hindrance from fibrous tissue In one specimen, actual overgrowth of smooth muscle is seen (fig 3, *A*) the significance of such hyperplasia is not understood

Figure 3, *B* shows almost complete reconstitution with little scarring although only 4 weeks had elapsed since operation Later specimens are similar with one exception (dog 116) in which bone was laid down beneath the new mucosa Muscle is absent in that area

Series C If urinary flow is permitted uninterruptedly (as previously reported[3]), smooth muscle repair is retarded even as long as 12 weeks after operation (table 3) While these results are not directly comparable to those in animals in which the ureteral walls were partially excised rather than held open, they do show that in the presence of continuous urinary flow, fibrous reaction is intense and completion of the repair by ingrowth of smooth muscle is delayed and inhibited (fig 4)

In summary of the results of these 3 series of experiments if urinary flow is prevented for a week, the epithelium has a chance to seal the defect When urinary flow is resumed, muscular regrowth is then not particularly deranged If permanent obstruction to urinary flow is obtained, reconstitution is even more rapid and orderly If urinary flow is not diverted at all, epithelization is delayed, fibrous reaction great, and smooth muscle regrowth inhibited

DISCUSSION

The data indicate that the flow of urine delays healing of the ureteral defect The effect is greatest if flow is continuous and less if the passage of urine is delayed one week Healing is best if no flow at all is permitted

Inspection of these findings shows items of significance Ureteral epithelization in unsplinted defects is found not to be solid in one week, leakage and delayed healing occur even if urinary flow is diverted for this period The findings of other workers with *splintered* defects is at variance, since their work shows that epithelization is complete even at a week This may be evidence that the splint guides the epithelium to earlier closure

The second implication of these experiments is that movement and exercise of the healing defect are of less importance to good healing than freedom from pressure, irritation and extravasation This differs from the conclusions of Johanson[5] that urinary flow assures an adequate urethral lumen after the strip urethroplasty of Denis Browne Intermittent flow in the urethra under the relatively high pressure which occurs on urination is important in maintaining the lumen, the constant, weak peristaltic flow down the ureter merely causes extravasation which impairs the formation of a proper lumen

A similar contrast is in the work of Lary and Scheibe[6] who studied healing of the common bile duct after reanastomosis These workers noted an incidence of stricture of 40 per cent if the long end of the T-tube splint were kept open, but had no strictures if the end was occluded so that normal biliary flow was not interrupted In their experiments, a tight closure was achieved, so that extravasation did not occur These results then cannot be directly compared with the open ureteral defects under consideration If the ureteral epithelium were restored by the time urinary flow was resumed, a similar dilating action might be noted However, on release of the obstruction in our experiments repair was not watertight and extravasation was possible

SUMMARY AND CONCLUSIONS

Excision of half the ureteral circumference was done on 15 dogs Seven of these had temporary urinary "diversion" and 8 had permanent proximal ureteral occlusion Free urinary flow was permitted in 4 dogs with open ureterotomies

Permanent diversion allows early epithelization and reformation of the ureteral lumen, with consequent adequate smooth muscle regeneration

Temporary diversion allows better healing than does free urinary flow, but does not prevent some leakage with resultant abnormal healing

Urinary flow delays primary epithelization, retarding muscle regrowth and resulting in imperfect ureteral repair

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[6] Lary B G and Scheibe, J R The effect of rubber tubing on the healing of common duct anastomosis Surg , **32** 789, 1952

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LEIOMYOMA OF THE BLADDER CASE REPORT

W G SHULTZ

Leiomyomas small in size are frequent findings throughout the body in sites where smooth muscle is normally found Such tumors of sufficient proportions to produce symptoms and require surgical intervention are seemingly rare as far as can be learned from the literature

The first case report of leiomyoma of the prostate was made in 1876 by Lebec[1] The patient, aged 76, gave a history of inability to urinate, he died of pneumonia Necropsy showed a tumor arising from the middle lobe of the prostate that was found to be made up of smooth muscle and was designated as a myoma of the prostate

The second case was reported in 1924 by Damski[2] also as a myoma and also as arising from the prostate a large tumor weighing 180 grams, but the patient had no urinary symptoms to indicate prostatism

Bugbee[3] reported his first case in 1926 and in June 1948 McIntyre[4] reviewed the literature and reported the twenty-second case Carson[5] in 1950 discovered two more cases in the literature and reported one which brought the total to 25 Carson first saw his case in November 1948 I first saw the patient whose case is herewith reported in February 1949 and operated upon him in March 1949 Therefore I am reporting the twenty-sixth case unless I have missed others

CASE REPORT

Mr G H L, aged 74, was first seen by me February 20, 1949 in consultation with Dr Frank T Hogeland in the Cananea Copper Company Hospital, Cananea, Sonora, Mexico The patient's major complaints were difficulty of locomotion, breathing and finding a place for his food His only urinary complaint was frequency A glance at figure 1 readily explains that symptom He had no difficulty in starting the stream, which was of good size and force No residual urine was present

The patient had noticed a tumor mass in his lower abdomen sometime previous to 1941 when he reported to doctors in Del Rio, Texas where a vas ligation was done by the then famous Brinkley organization On July 3, 1943 he consulted a surgeon in El Paso, Texas (the patient was then aged 66) who found in the lower abdomen a mass which extended above the pubis to the umbilicus and noted also that the umbilicus was discolored and very tender The bladder functioned well and no residual urine was present The prostate was large, soft and apparently connected in some degree with the tumor mass on the right, probably at the upper pole At cystoscopy when the bladder was entered, the instrument

Accepted for publication January 21, 1957

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Damski A Grosses Prostatamyom ohne Erscheinungen des Prostatismus Ztschr f urol chir 16 47 1924

[3] Bugbee H G J Urol 16 67 1926

[4] McIntyre D W J Urol 59 1198 1948

[5] Carson R B J Urol, 64 373 1950

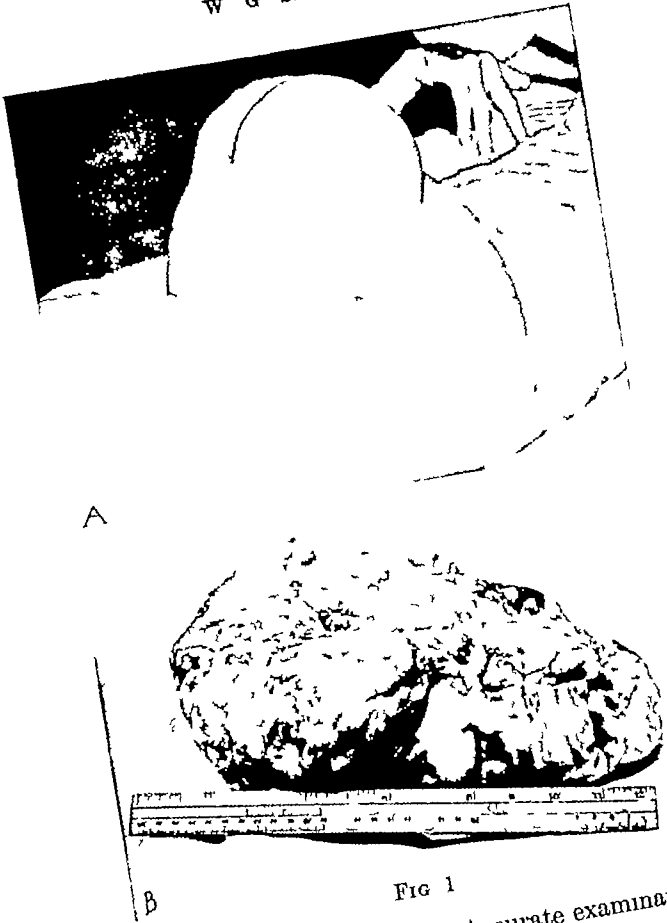

FIG 1

was pushed over to the patient's left side Accurate examination was impossible because of compression of the urinary bladder due to the mass on the right side

Urinalysis revealed one plus albumin, 150 pus cells per low powered field and 8–10 red cells The red blood count was 3,760,000, hemoglobin 11 5 gm The white count was normal Spinal fluid was negative, Kahn negative, red blood cells 1,000, white blood cells 51, globulin negative The surgeon made a provisional diagnosis of tumor of the bladder, probably extrinsic, probably carcinoma of the prostate or carcinoma of the urachus An account of his operation follows

Operation (July 5, 1943) Incision was made midline just below and above the umbilicus, the umbilicus being excised After the peritoneum was opened, above this point, the umbilicus was seen to be connected with very large blood vessels running upward from the tumor mass The tumor was extraperitoneal, hard and solid, and filled practically the entire pelvis, posteriorly it was adherent to the rectum, and anteriorly on sides It was densely adherent to the lateral walls of the pelvis It was apparently inoperable

An attempt made to excise a piece of the tumor for biopsy was impossible, as not only the surface of the tumor, but in the various layers of the mass huge thick walled veins were present and no point could be found from which to excise a piece for examination The umbilicus with attached blood vessels from the tumor was kept for this purpose The peritoneum was resutured and wound sutured over tumor

Pathological report The gross specimen consisted of an umbilicus, with a small fragment of the surrounding skin It measured 7 by 2 cm Attached to the deep surface was a very vascular mass of fibrofatty tissue Thin walled blood vessels were numerous and large The tissue was firmly adherent to the peritoneal surface immediately underneath the umbilicus It was rather soft in consistency throughout

Microscopic study revealed that the tissue adherent to the umbilicus was composed of dense connective tissue, fatty tissue, and many blood vessels of moderate size Connective tissue spaces contained focal collections of lymphocytes and plasma cells No structures resembling tumor tissue were visible in the section studied Diagnosis Fibrofatty tissue from peritoneal cavity

The patient had an uneventful convalescence and was sent to his home with a tentative diagnosis of inoperable carcinoma and hopeless prognosis

The tumor mass grew slowly and the patient gradually became more uncomfortable chiefly due to encroachment of the mass upon the abdominal organs He became discouraged because he had not died and wished to have an effort made to relieve his uncomfortable condition even at the risk of death which he was warned might follow an attempt to remove the enormous mass Dr Hogeland felt that the growth was not cancerous and it was my opinion, after examination, that the mass was an adenoma or myoma The patient refused to come to Tucson for operation and I agreed to operate upon him in Cananea with Drs Hogeland and Gonzalez assisting

Operation (March 20, 1949) Under ether anesthesia, the enormous tumor shown in figure 1 was removed When we got down into the bony pelvis the mass was tightly wedged, segmental removal had to be resorted to and at least 1000 cc serous fluid was lost from the tumor (It probably amounted to more but we were not aware that we were going to encounter it and the mass was ruptured before measuring devices could be obtained) A considerable amount of hemorrhage was encountered and the patient received blood throughout the procedure When the base of the mass was removed, it was found that a small tear had occurred at the base of the bladder, on the right side at the point where it could be expected to join the prostate gland The patient's condition was such that I did not take time to make the examination required to prove whether the mass came from the wall of the bladder or the prostate itself A Foley catheter was placed through the urethra into the bladder before closure of the tear in the vesical wall and the abdominal incision closed in the standard manner

The patient succumbed approximately 8 hours following surgery

The gross specimen (fig 1, *B*) weighed 3 5 kilograms without the fluid which it contained Each segment of the specimen, although it had been removed segmentally, was fitted back into the position it formerly occupied and sutured in position for the purpose of the photograph The pathologist's report on three segments taken from different parts of the growth follows

The gross specimen presented for biopsy weighed 16 5 gm and was presented as three, formalin-fixed, irregularly-shaped, rubbery masses of tissue which were fibrous in texture, sections revealed the presence of an occasional, irregularly-shaped small cavity which did not appear to possess an epithelial lining but was filled with serous fluid

Routine paraffin sections were stained with (a) hematoxylin and eosin, and (b) according to the Van Gieson technique The tissue was not richly vascular but contained rather numerous scattered blood vessels which possessed walls of capillary thinness An abundant hyaline matrix had scattered in its spindle shaped cells, the majority of which resembled those of histiocytes Also scattered in this matrix were fairly numerous and widely distributed cells which appeared as plasma cells but were occassionally swollen so that they resembled Russell bodies No mitotic figures were seen In certain regions, about the margins of the cavities, the tissue showed marked karyolysis, there was liquefactive necrosis without associated leukocytic infiltration With the Van Gieson stain, the matrix presented a yellow-tinted background with wavy, delicate collagenous fibers which ran in all directions, the picture simulating that of ordinary degenerating uterine "fibroid " Diagnosis Degenerating large leiomyoma, presumably of prostate gland (fig 2)

Comment Inasmuch as this observer has never before encountered a leiomyoma of the prostate gland approaching this size, sections and "wet tissue" will be submitted to Dr R A Moore, professor of pathology, Washington University School of Medicine Signed Ralph H Fuller, M D , pathologist

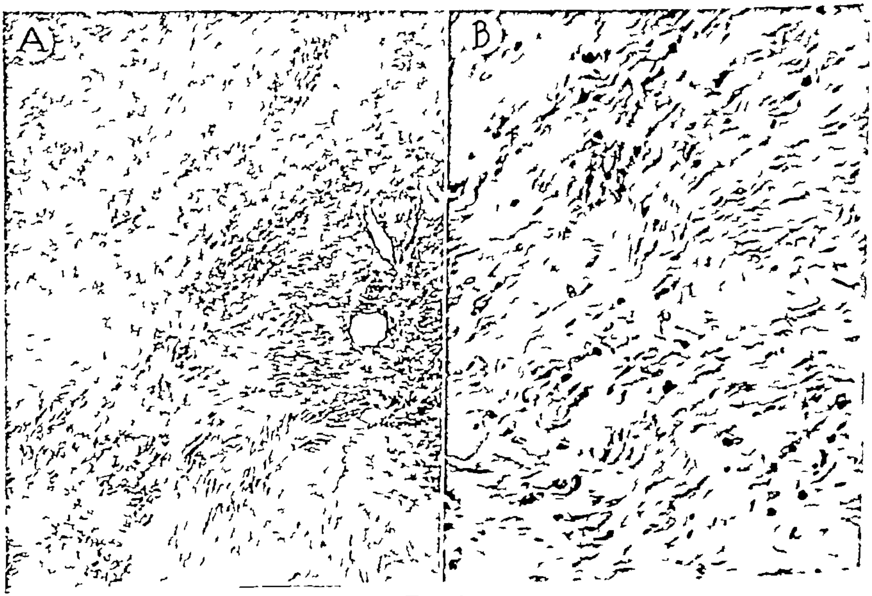

FIG 2

Pathology report from Dr R A Moore, professor of pathology, Washington University

"I concur in your diagnosis of presumably a leiomyoma of the prostate which is undergoing degenerative change This type of degenerative change occurs in both the prostate and in hypertrophied prostate, and when extremely cellular, takes on some of the appearances of sarcoma However, experience has shown that this is not a malignant tumor Leiomyomas of the prostate of the size you report (4 kilograms) are unusual, but I know of no reason why this tumor should not occasionally be seen of large size As you already know, it is my own opinion that leiomyoma of the prostate is only one of the variations of the basic diagnosis, nodular hyperplasia In some instances, it is composed largely of glands, in some exclusive of stroma, and in most is both"

SUMMARY

Irradiation therapy certainly should have been tried in this case, in the earlier stages at least The patient would not leave his home town, and deep x-ray therapy was not available there

A case of what I believe can be termed an enormous leiomyoma, probably of the bladder, possibly of prostatic origin, is herewith presented No symptoms of urinary obstruction were present

Therefore, it is my opinion that the tumor arose from the right wall of the bladder at a point near the prostate

1010 North Country Club, Tucson, Ariz

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SENILE URETHRITIS IN WOMEN

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Senile urethritis in women is an atrophic lesion of the urethra due to a deficiency of endogenous ovarian hormone and manifested by irritative symptoms of the lower urinary tract We could find no direct reference to this condition in the periodical medical literature, although it is mentioned occasionally in textbooks However, urologists for years have recognized senile changes in the female urethra and have used various types of replacement therapy

Youngblood[1] has shown previously that chronic nonspecific urethritis in women is a common finding, and that it responds well to treatment with furacin urethral suppositories * Similarly favorable results were later reported by Gomberg[2] and more recently by a number of other clinicians [3-6]

From 1951 to 1954, one of us (V H Y) treated all cases of urethritis in women with furacin urethral suppositories Analysis of some 1,200 case records revealed that premenopausal women almost invariably were improved, but a high percentage of postmenopausal women were not Furacin urethral suppositories, with added 0 1 mg diethylstilbestrol each, were then tried in 25 postmenopausal women who had previously been treated without success All subjective and objective symptoms were promptly relieved This led to the present investigation

SIGNS AND SYMPTOMS

3 The subjective symptoms of senile urethritis do not differ from those of other inflammatory conditions of the lower urinary tract except that a large proportion of patients have dyspareunia, as is also common in nonspecific urethritis
2 Urethritis is probably the main cause of dyspareunia

On examination, the vagina may or may not show senile vaginitis Eversion of the urethral mucosa at the meatus is almost pathognomonic, but must be differentiated from prolapse and caruncle Endoscopy reveals that the urethral mucosa is atrophic, inelastic, hyperemic, and bleeds easily There are no specific characteristics of senile urethritis, endoscopically it is almost indistinguishable from nonspecific urethritis

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Accepted for publication February 19, 1957

* Furacin urethral suppositories contain 0 2 per cent furacin (Eaton Laboratories' brand of nitrofurazone N F) and 2 per cent diperodon HCl (a topical anesthetic in water soluble base)

[1] Youngblood, V H Nitrofurazone in the treatment of nonspecific urethritis in women J Urol, 70 926–929, 1953

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[3] Tudor, J M Chronic posterior urethritis in the female J Tenn M Assoc, 49 181–195, 1956

[4] Hughes, J, Coppridge, W M and Roberts, L C Office management of urinary tract infections North Carolina M J, 17 320–325, 1956

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[6] Flocks, R H and Kadesky, M D The medical management of urinary tract infections Med Clin N Amer, 40 1545–1553, 1956

CLINICAL MATERIAL AND RESULTS

From February 1955 through August 1956, the senior author treated 329 new female patients with urethritis. Their ages ranged from 1 to 102 years, the average age being 55 years. Of these 329 women, 252 (76 per cent) were postmenopausal.

Eaton Laboratories supplied us with five different types of urethral suppositories, designated only by code letters so that their compositions were unknown. All five types of suppositories had the identical suppository base. Initially these five types were used in rotation.

All women with urethritis demonstrable by endoscopy were instructed how to insert suppositories and were given a supply for self insertion twice daily. Sitz baths twice daily were also prescribed. To prevent retrograde cystitis following any minor trauma during self insertion, furadantin 50 mg t.i.d. per os was given. No such cases of cystitis developed. After 1 or 2 weeks' treatment, the urethra was dilated if endoscopic findings indicated it. Postmenopausal women were maintained on one or two suppositories a week thereafter, since senile urethritis was found to recur unless medication was continued. Patients were then seen at intervals of 2 or 3 months.

Suppositories A and C were soon discarded in the senile urethritis group. Type A showed excellent results in nonspecific urethritis of premenopausal women, but no results in the postmenopausal group of patients. This suppository proved to be the standard furacin urethral suppository. Type C produced no improvement in either group. This was a blank control.

Type B suppositories produced objective benefit, but were uncomfortable for the patient to use, and their use was abandoned after treatment of about 20 patients. These contained 0.1 mg. diethylstilbestrol without either anesthetic or antibacterial agents.

Excellent results were obtained in postmenopausal women with types D and E. Type D suppositories were used in 112 patients with senile urethritis and improvement was noted in all. This type also brought some improvement in patients with nonspecific urethritis, but such improvement was much less definite than in the senile urethritis. Type D contained 0.1 mg. diethylstilbestrol and a topical anesthetic agent, 2 per cent diperodon HCl, in water-dispersible base identical with that used in furacin urethral suppositories.

Type E suppositories were employed in 120 cases of senile urethritis. All of these patients showed more rapid improvement than those treated with type D, although the degree of improvement could not be measured objectively. Treatment of nonspecific urethritis with these suppositories brought results similar to those previously reported[1, 2] with furacin urethral suppositories, but the rate of epithelization appeared more rapid. Type E was the standard furacin urethral suppository, containing in addition 0.1 mg. of diethylstilbestrol.

In every patient with senile urethritis, treatment with estrogen-containing suppositories was followed by improvement as demonstrated by disappearance of endoscopic signs of urethral irritation, disappearance of senile vaginitis, diminution in size of bladder neck polyps when present, and an increased elasticity of the urethra as observed on sounding. Some patients required additional treatment for such conditions as caruncle, bladder neck contracture, cystocele, etc , but 91 per cent were relieved with suppository treatment alone

Furacin urethral suppositories with diethylstilbestrol proved effective in both chronic nonspecific and senile urethritis in women Urethral insertion of the suppositories containing estrogen was sufficient to relieve associated senile vaginitis, in most cases They were also found effective in several cases of juvenile vulvovaginitis, a condition which also responds to the standard furacin urethral suppositories as previously reported by Carroll[7] and Lang[8] Some cases of urethritis in men, and proctitis, also responded well

The histologic changes of senile urethritis are now being studied by use of Papanicolaou's stains of exfoliated cells of the urethral mucosa Preliminary results show that in the first 12 cases so studied, a healthy stratified squamous epithelium regularly replaced the atrophic urethral epithelium after 2 weeks' topical therapy with furacin and diethylstilbestrol This parallels the well known effect of estrogens in the senile vagina A complete report of this study is in preparation

SUMMARY

Of 329 new cases of female urethritis, 76 per cent were postmenopausal, indicating that most of such cases may be due to deficiency of endogenous ovarian hormones Furacin urethral suppositories generally gave good results in premenopausal women only In senile urethritis, excellent results were obtained with the same suppositories containing in addition 0 1 mg diethylstilbestrol A preliminary study with Papanicolaou smears of exfoliated urethral cells showed progressive histologic change during treatment Nonspecific urethritis likewise improved during treatment with suppositories containing both furacin and diethylstilbestrol

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[7] Carroll, G Chronic urinary infections in infants and children Pediat Clin N Amer , pp 781–791 (Aug) 1955

[8] Lang, W R Pediatric vaginitis New Eng J Med , **253** 1153–1160, 1955

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PRIMARY PRIAPISM A NEW TREATMENT

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Primary priapism is defined as a sustained, painful pathological erection unaccompanied by sexual desire and involving only the corpora cavernosa[1, 2] Priapism has occurred in a multitude of conditions which have been discussed elsewhere[1, 3-8]

Best and Taylor[9] described the phenomenon of erection as an increase in blood volume in the corpora secondary to vasodilation of the internal pudendal artery with contraction of the involuntary muscle at the venous-sinusoid-capillary level There is evidence that an arteriovenous anastomosis also exists which opens to increase the blood flow into erectile tissue Wiggers[10] believes that erection is due not to involuntary muscle contraction but rather to the mechanical leverage action of the suspensory ligaments attached to the posterior portion of the cavernous bodies Regardless of the exact mechanism of erection, McKay and Colston[11] have noted in priapism the presence of a thick sludge of unclotted blood in the sinusoids of the corpora cavernosa

Treatment is varied as in any syndrome whose pathological mechanism is poorly understood The use of sedation, anesthesia of all types, hypnosis, and estrogen administration have met with almost universal failure McKay and Colston[11] report successful treatment of priapism with aspiration and irrigations of the corpora cavernosa with saline The treatment is often complicated by infection, and recurrence of priapism is frequent

In the case reported here, we utilized a new technique not previously described in the literature The procedure consists of heparinization of the patient for 4 days, followed by forcible massage of the penis under general anesthesia We are gratified by the immediate reduction of erection and subsequent absence of pain and surgical complication Unfortunately, the patient is still impotent It is our hope that earlier forcible emptying of the corpora will avoid this complication

CASE REPORT

J S , a 40-year-old married Puerto Rican man, was admitted to San Francisco Hospital on February 1956, complaining of painful erection of 5 days' duration

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The patient was in good health until 5 days prior to admission when he noted the gradual onset of painful erection The patient ordinarily engaged in three to five copulations per week He denied any abnormal prolongation of erection On the day prior to the onset of priapism he had had sexual intercourse twice

On examination, temperature was 98 6F and blood pressure 150/84 The patient, a well developed man, complained of pain in the penis if he moved or if the bed clothes touched the organ The penis was in severe rigid erection without deviation and palpation revealed exquisite pain in the bulb The color of the skin was unremarkable and the glans was not involved The prostate was normal Neurological examination was within normal limits

Hemogram and urinalysis were normal The blood serology was negative Nonprotein nitrogen was 27 mg per cent Two traumatic spinal punctures revealed a cerebral spinal protein of 99 and 83 mg per cent

Ethyl chloride spray, spinal anesthesia and sedation were not effective in reducing the priapism Ten days after admission, the patient was given heparin sodium 50 mg intramuscularly every 6 hours for 4 days On the fourth day, he was taken to the operating room and given a general anesthetic The corpora cavernosa were forcibly massaged from the glans to the bulb, using the thumb and forefingers of both hands This procedure took about ten minutes Immediately after the stripping, the penis became blue and semi-flaccid Thereafter, varidase 5000 u was given intramuscularly 4 times a day for 4 days For the next 10 days, the penis was edematous and semi-flaccid, but painless The patient had no difficulty in micturition at any time and his postoperative course was afebrile At the time of his discharge, the penis was practically flaccid and was normal in appearance

At examination 2 months later the penis appeared normal but the corpora were firm The patient was impotent One-year followup showed persistence of impotency

SUMMARY

A case of primary priapism treated with a new technique is presented The patient was relieved without surgical intervention

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CONGENITAL ABSENCE OF THE PENIS CASE REPORT

JURGEN R HALLER, LEROY B SCHUMAKER AND TERRANCE D FURNESS

A review of the literature shows that absence of the penis is a rare congenital abnormality The purpose of this paper is to add one case to the twenty-one confirmed previously reported cases

Embryologically the absence of the penis and urethra apparently is failure of the genital tubercle to form or its failure to form a phallus and the anterior urethra The absence of the proximal urethra is due to the absence or failure of development of the vesicourethral anlage and the urogenital sinus (Arey)

A communication between the bladder and the rectum or the anus, found in many cases, is due to persistence of the cloacal passage and failure of the urogenital sinus to reach the cloacal membrane

TABLE 1

1	Imminger	1853	11	Feller and Sternberg	1938
2	Nelaton	1854	12	Rukstinat and Hasterlik	1939
3	Goeschler	1859	13	McCrea	1942
4	Collier	1889	14	Lal	1943
5	Rouber	1890	15	Gillies (2 cases)	1948
6	Mathews	1893	17	Bolasquide	1950
7	Harris	1898	18	Campbell (2 cases)	1951
8	Magid	1929	20	Bernardinelli	1953
9	Priesel	1931	21	Stoll	1954
10	Drury and Schwarzell	1935			

More than one-fourth of the patients listed in table 1 died within a few hours after delivery They all had severe coexisting anomalies which were not compatible with life In three cases the bladder ended blindly In another the prostatic urethra terminated in an obliterating membrane which was connected to the wall of the rectum Four presented atresia of the rectum and the anus or the anus only More than three-fourths of all cases showed coexisting anomalies, such as hydrocele, atresia of ureters, hydroureters, hydronephrosis, absence of the prostate gland, pelvic deformities, atelectasis of lungs, hepatomegaly and malformation and atresia of the colon, rectum and anus The scrotum was present in all cases

The condition must be differentiated from "hidden" or "concealed" penis, pseudohermaphrodism, rudimentary penis and severe hypospadias

The following is the twenty-second authenticated case in the literature

CASE REPORT

On September 15, 1955, a 34-year-old white gravida 3, para 2 female in strong labor was admitted to the delivery floor of Mercy Hospital

Examination indicated fetal distress evidenced by meconium stain, amniotic fluid and a fetal heart rate of 90 per minute between pains Under ether anes-

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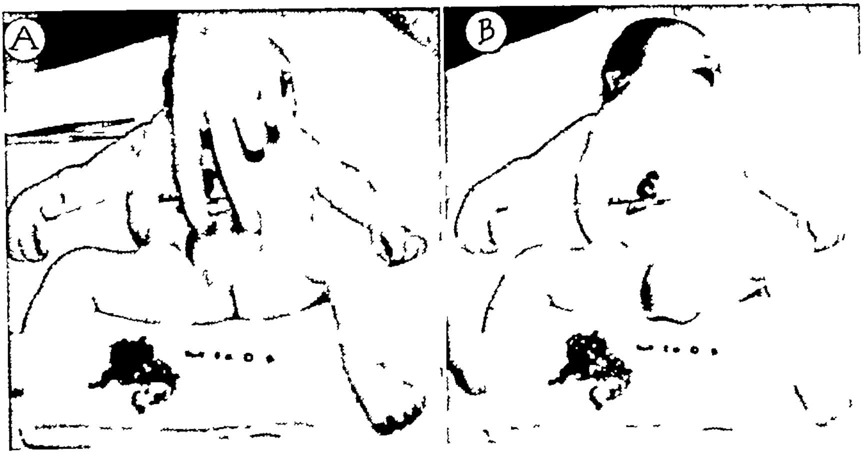

FIG 1

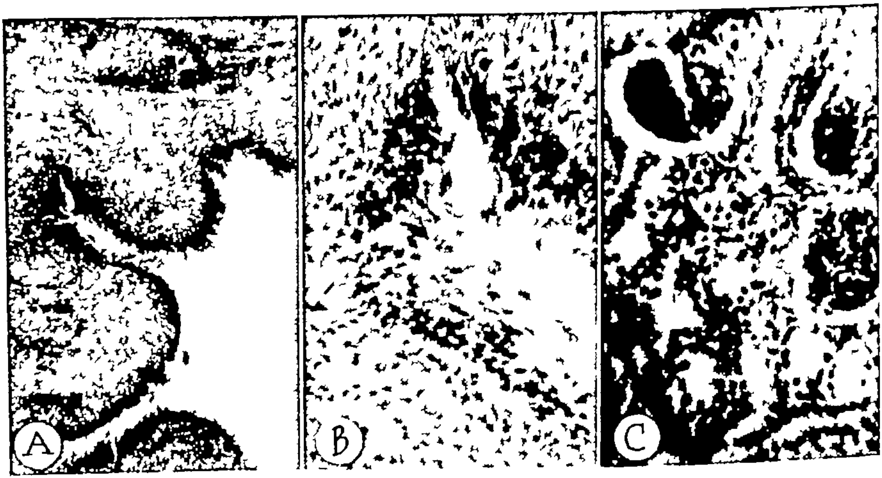

FIG 2

thesia, with forceps, the patient delivered a 7 pound, 11 ounce living male The placenta was greenish discolored when expelled The infant was lethargic and responded poorly to artificial respiration and oxygen He was transferred to the nursery and placed in an incubator

On physical examination complete absence of the penis was noted The scrotum and raphe were well formed Both testicles were descended and of normal size (fig 1) No urethral orifice could be detected The chest was full of rales Respirations remained short and gaspy Liquid meconium stools and pea-sized masses of meconium and mucus were expelled at intervals from the rectum No urine was excreted from the anus at any time After 7½ hours the infant became cyanotic, respirations irregular, and the patient finally expired Surgery was not attempted because of the extremely poor condition of the infant

Autopsy report The kidneys showed fetal lobulations The capsules stripped easily The ureters communicated normally with the bladder The bladder was elongated, not distended, contained no urine and ended blindly Besides agenesis of the penis and the urethra there was a congenital megacolon, hypertrophy of the right ventricle of the heart, hepatomegaly, and partial congenital atelectasis of both lungs

Microscopic examination The bladder was removed as one block together with its surrounding tissues Serial sections of the bladder did not reveal a urethral orifice The mucosal side of the bladder presented a wrinkled condition which was compatible with the gross observation that the bladder was not distended Transitional epithelium could be identified (fig 2, *A* and *B*) The embryonic kidney showed imperfect formation of the tubules, the glomeruli were not mature, the tubules devoid of urine (fig 2, *C*)

SUMMARY

The evidence and history of congenital absence of the penis are discussed briefly

One case of congenital absence of the penis is presented which is confirmed by autopsy and histological examination

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PARATESTICULAR INTERSTITIAL CELL TUMOR IN A BOY AGED ELEVEN

WILLIAM A BARRETT

Interstitial cell tumors in children produce little men much before their time Because of the precocious genital development and premature secondary sex characteristics associated with unusual muscular development, these children arouse great concern of their parents and an unusual interest in the profession

A tumor that is not in the testis is not truly testicular but, composed of cells characteristically found in the testicle, and, lying adjacent to that organ, it can be called a paratesticular interstitial cell tumor Since all of the tumors except the one reported by Tedeschi and Burke were within the testes, our finding of a paratesticular interstitial cell tumor in a boy 11½ years old seemed worth recording

Friedman and Moore have said that testicular tumors make up only 0 5 to 2 0 per cent of all cancers in the male and this specific interstitial cell tumor constitutes only one per cent of this small group Lewis, in a series of 922 cases found nine instances of interstitial cell tumor They have been reported with greater frequency in the past 14 years but only a total of about 56 cases have been authenticated or accepted by the majority of investigators and about six other cases mentioned by the various reporters Of this total, sixteen (table 1) were found in children before the age of puberty Six were definitely malignant (Gharpure, de Josselin de Jong, Masson, Masson and Sencert, Nation, Edmondson and Hammack) and all of these in adults, in one of which metastases appeared 9 years after removal of the primary tumor and 10 years after its original discovery Each case in which metastases developed was fatal Three cases reported were bilateral (Flynn and Severance, Garvey and Daniel, Staubitz, Oberkircher and Blick)

HISTORICAL

Leydig in 1850 first described the interstitial cells of the testes and Waldeyer in 1872 directed attention to tumors derived from the interstitial cells Most writers have generally accepted the case reported by Sacchi in 1895 as the first authentic interstitial cell tumor of the testis reported

An extensive revision of the literature has been carried out by many and some cases have been questioned by various writers (Huffman, Jemerin, Melicow, Robinson, Ivers and Rainsford) Several reported seemed to have been eliminated on the basis of being simple hypertrophy of the interstitial tissue or tumors unrelated to these cells Those which are generally accepted to date total 39 adults and 16 children with six additional adult cases being considered possibilities The case herewith presented brings these totals to 39 and 17 respectively (table 1) This is only the second such tumor, however, to be found outside of the testis

Read at annual meeting, Northeastern Section of American Urological Association, Lake Placid, N Y , September 9, 1955
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TABLE 1 *Interstitial cell tumors in children*

	Year	Age		Hair on				Acne	Endocrine Changes
		First seen	On set	Chin	Chest	Axilla	Pubis		
1 Sacchi	1895	9	5½	−	−	−	+		Macrogenitosomia
2 Rowland and Nicholson	1929	9	6	+	+	−	+		Macrogenitosomia
3 Sutherland	1932	11	5	+	−	−	+	+	Macrogenitosomia
(Somerford)	1941	(Same Case as Sutherland)							
4 Stewart et al	1936	5	4	−	−	−	+		Macrogenitosomia
5 Huffman	1941	6	4	−	+	−	+		Gynecomastia Macrogenitosomia
6 Werner et al	1942	6MI	5½	+	−	+	+		Macrogenitosomia
7 Rezek	1943	10		−	+	+	+		Macrogenitosomia
8 Anderson	1946	6		−	−	+	+		Macrogenitosomia
9 Melicow et al	1949	5	4½	−	−	+	+		Macrogenitosomia
10 Fraser	1949	4	2	−	−	−	+		Macrogenitosomia
11 James and Shupe	1950	14	9	−	−	−	+		Macrogenitosomia
12 Cook et al	1952	5	4	+		+	+	+	Macrogenitosomia
13 Anagnostou and Frangopoulus	1953	6½	4	+		+	+		Macrogenitosomia
14 Staubitz et al	1953	3	3	−	+	−	+		Macrogenitosomia
15 Hertz et al	1953	5	4	−	−	+	+	+	Macrogenitosomia
16 Pomers et al	1954	7	6½	−	−	−	+		Macrogenitosomia
17 Barrett	1955	11½	4	+	+	+	+	+	Macrogenitosomia

CASE REPORT

W B W , aged 11½ years, a white boy, was first examined on November 18, 1952 He had been referred by the school physician indirectly because of his unusual development and because "he had three testes " At age four, the parents had noticed enlargement of the penis and growth of pubic hair At 4½ years there was considerable increase in his weight with what appeared to be edematous tissue and this was diagnosed at the Children's Hospital as having been due to a kidney condition He was said to have had a severe "cold" just previous to the beginning of these unusual developments at age four The penis gradually increased to adult size, his voice became deep and resonant and his muscular development was rapid At 7½ the facial hair became quite prominent as did the hair on the rest of his body At nine he began to shave and, for one year prior to examination, had been shaving twice each day Frequent erections had been noted and repeated emissions of seminal fluid were admitted

For 2 years previous to this examination, the patient had noted a swelling in the left scrotal sac which was "about the size of a walnut," but gave no pain or discomfort, and it was this tumor which the examining school physician thought might be a third testis

At age 4 years, 10 months he had been admitted to the Children's Hospital with the complaint of swelling of the face for 6 months It was noted then that he was large for his age ' and 'appeared rather precocious " "His external genital development exceeds that of his years and he has a dermatitis resembling adolescent acne." There was also a slight increase in pubic and axillary hair. X-rays showed a "bone age of 6 years" and a "rather small sella turcica." At that time the serum protein was 7.8 mg., serum albumin 5.7 mg. and serum globulin 2.0 mg. 17-Ketosteroids had not been determined.

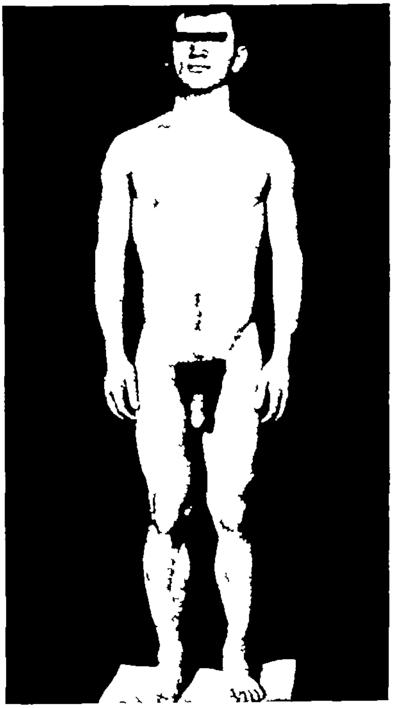

FIG. 1. Note adult proportions of an 11 year old boy's physique changed by interstitial cell tumor. Face is that of a man, muscular development that of a man, length of legs less than that of torso, hair growth of pubis and legs that of an adult, as are also external genitalia.

Examination showed the boy to have the general appearance of one approximately twenty years of age (fig. 1) but his height was 61¾ inches and the weight 129½ pounds. The head and face were those of an adult with a very heavy black beard and considerable evidence of acne which had been present for quite a while (fig. 2). His muscular development was that of an adult. Chest and shoulders were well developed and a moderate amount of black hair covered his chest, arms, and legs. The pubic hair was black and that of an adult male in distribution and amount. The penis was of adult size measuring 9.0 cm. and partially turgid when first examined. Both testes were normally placed, measured 2.0 by 1.5 cm. and of average consistency. The epididymides appeared normal. In the left scrotal sac, lying about 1.5 cm. from the testis and slightly above it, was an ovoid mass measuring about 4 by 3 cm. which was solid and neither fixed nor tender. It did not seem to be attached to the cord and no adenopathy was palpable in the inguinal areas. The prostate and seminal vesicles were slightly larger than normal for this age and approximately that of a young adult.

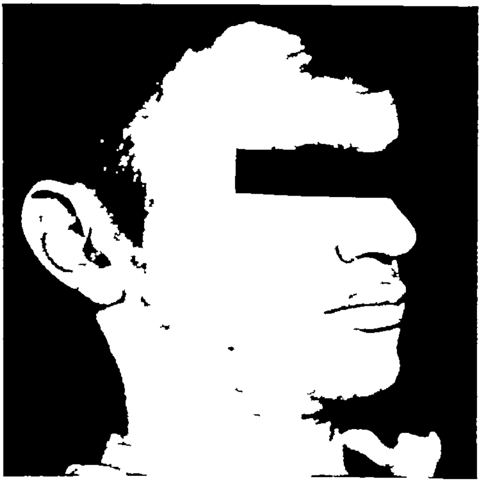

FIG 2 Facial proportions those of an adult Heavy dark beard and evidences of chronic acne are prominent

The routine laboratory studies were normal Urine was clear, had a specific gravity of 1 022, a pH of 5 0 no albumin and no sugar An occasional epithelial cell and two to three white blood cells were found per high powered field The blood picture showed 4 6 million red blood cells 90 per cent (14 0 gm) hemoglobin 8,800 white blood cells, 66 per cent neutrophils, 1 per cent eosinophils 30 per cent lymphocytes and 3 per cent monocytes The nonprotein nitrogen was 30 mg per 100 cc and blood sugar 92 mg per 100 cc

An intravenous urogram was taken immediately after the injection of presacral oxygen and indicated normal function of both kidneys which were in normal positions No abnormal excursion was found The calyces and pelvis on each side were well visualized normal in contour and not retentive The retroperitoneal oxygen well delineated both kidneys and adrenals and did not suggest the presence of tumor in or displacing these organs

A stereoscopic examination of the sella turcica showed no enlargement, no evidence of demineralization of the posterior clinoids and no evidence of erosion of the floor X-rays of the wrists and ankles showed the epiphyses for the distal end of the radii and ulnae to be almost closed The epiphyseal lines in the proximal end of the first metacarpal bones could not be identified This placed the bone age at approximately sixteen years

Twenty-four hour urine specimens sent to the laboratory for 17-ketosteroid examinations prior to operation were lost and no preoperative determination was obtained (Tedeschi and Burke)

At operation an ovoid shaped, dark, firm tumor mass was found within the left tunica vaginalis testis completely separate from the testis and slightly above it The blood supply to this mass was entirely separate and greater than that which supplied the testis and epididymis They were normal in size, appearance, and consistency for this age and showed no areas of induration or tumor mass within them

The report of the pathologist, Dr Richard McManus, was as follows "The specimen (fig 3) consisted of a thinly encapsulated, glistening, smooth, red, ovoid mass measuring 4 2 by 2 6 by 1 8 cm The cut surface was dark red, of uniform appearance throughout and tended to bulge slightly Microscopically (fig 4), the tumor was composed of large polyhedral cells with abundant eosinophilic, finely vacuolated cytoplasm and centrally located round or oval nuclei One or two definite dark nucleoli were usually found These cells were arranged in the form of trabecular cords and strands with fibrous septa between them No mitoses were seen Many cells were heavily pigmented with brown pigment There was penetration of the tumor cells into the capsule but no blood vessel invasion was seen " A section was specially stained with Sudan to show the lipoid content (Huggins and Pazoa, Mayers) and granules, and another with malachite green to illustrate the strands of fibrous tissue

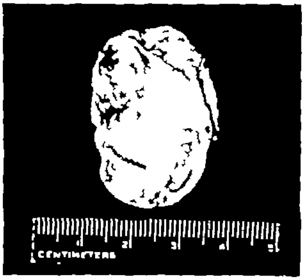

FIG 3 Excised tumor smooth, red, ovoid and measured 4 2 by 2 6 by 1 8 cm Cut surface dark red, of uniform appearance and tended to bulge slightly

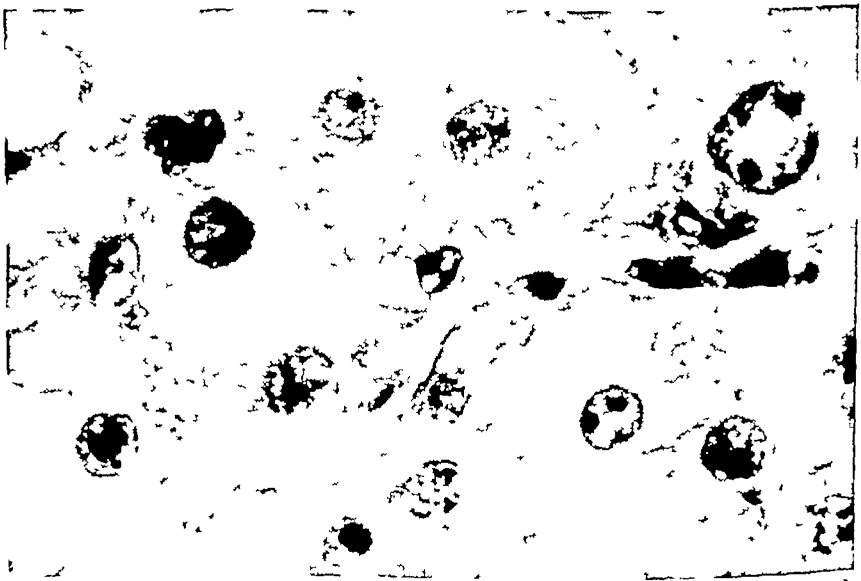

FIG 4 Microscopic section shows large polyhedral cells with abundant eosinophilic, finely vacuolated cytoplasm and centrally located round or oval nuclei One or two definite nucleoli are usually found No mitoses are seen Many cells heavily colored with brown pigment

The patient has been observed and followed every three to six months since operation His general appearance is unchanged and there is little change in his measurements The height approximately three years after operation is 5 feet, 2 inches and his weight approximately one hundred and forty pounds The acne of the face is almost entirely gone and his beard is somewhat lighter He now shaves every day or two The hair of the body is unchanged and the size of the penis is the same as before There is some increase in the size of the right testis but the left testis appears to be approximately the same size as when operation was performed On April 11, 1955, the 17-ketosteroid determination was 19 2 mg for 24 hours, and now 9 4 mg per cent

DISCUSSION

The youngest case recorded of this type was 2 years of age (Frazer) and the oldest 82 years with the greatest incidence in children between 4 and 6 years, in adults, between 30 and 45 years Those cases which seem to have begun after puberty are characterized primarily by the presence of a tumor mass in the testis No constant changes in their secondary sex characteristics have been noted and in only three instances were the presence of gynecomastia noted (Hunt and Budd, Mayers, Melicow) and one in a child aged eight (Huffman, Nation, Edmondson and Hammack) Melicow has reminded us that "gynecomastia occurs under a variety of conditions and is not pathognomonic of any one particular endocrine dyscrasia " Three cases were accidently found at autopsy (Bonser and Hawksley, Lopis, Bothwell and Swendlow) with no genital changes other than the size of the tumor mass in the testis In three instances (Chevassu, Jemerin, Price) the tumor developed in an undescended testis

When these tumors developed before puberty attention was usually directed toward them because of the endocrine changes resulting in 1) macrogenitosomia which occurred in every one of the seventeen reported cases, 2) gynecomastia which occurred in only one (Huffman), 3) the growth of hair on chin, chest, axilla and pubic areas, and 4) the deepening of the voice When these changes have been present over a considerable period of time, there were also 5) an acne of the face, 6) heavy muscular development, and, 7) closure of the epiphyseal lines

Following operation, several authors have reported almost a complete recession of secondary sex characteristics, approximately one-third noted only slight amount of change and the majority by far report no change whatsoever The extent of recession of these changes postoperatively would seem to be dependent upon the age at which the tumor began to develop and the number of years its hormonal secretions had been permitted to exert their effects upon the other tissues

Interstitial cells are said to be numerous in the fetus and decrease again during adult life only to reappear again as senility sets in and the seminiferous tubules atrophy This last increase, however, is believed to be relative

Fraser says the interstitial cells first appear in a 19 5 embryo "probably as a result of the transformation of mesenchymal cells (Maximow 1947) " In the later half of gestation they decrease relatively in number Arey says that ' the general bed of mesenchyme in which the tubules of the testis lie, organizes into the connective tissue framework of the organ Thus, each lobule of the testis, containing the three or four seminiferous tubules derived from a primitive testis cord becomes isolated by portions In one direction, these septula converge to the mediastinum testis (enclosing the rete tubules), in the opposite (peripheral) direction they extend to the encapsulating tunica albuginea Certain cells of the mesenchymal stroma transform into large, pale elements which lie in the unspecialized connective tissue between the seminiferous tubules and hence are designated interstitial cells They are very abundant in the fourth month and again increase in number after puberty " Warren says "the presence of interstitial cells around the body and tail of the epididymis and along the arteries intimately associated with the nerves near the mediastinum testis (corpus highmori) has been demonstrated by Altman, Masson and Sencert, and Maximow and Bloom " These anatomical observations would seem to explain why it is possible to find interstitial tumors outside of the testis proper The case of Tedeschi and Burke was the first such case to be reported

The neutral fat determination in these cells closely paralleled the staining properties with Sudan dye and these "are considered useful aids in the classifications of this category of tumors Seminomas are said to have a low fat content, whereas tubular adenomas from Sertoli cells and interstitial cell tumors have a high fat content "

According to Jemerin, "in the first state, the protoplasm is filled with high refractile granules, a large part of which represents neutral fat or lipoids Numerous brownish granules of varying size having properties of waste pigment (lipofuchsin) are present Other inclusions are droplets of colloid-like substance, granules of an indefinable nature and peculiar, heavy staining rod-like crystalloids with rounded or pointed ends known as Reinke's crystalloids " Grabstald et al also described them Whether due to the omission of the Romanowsky stain or whether it is a failure on the part of our later-day staining technique, the majority of cases reported fail to find the presence of Reinke's crystalloids Dixon and Moore in their monograph show a photomicrograph containing two alleged crystalloids between the cells

It is the presence of lipoids which causes the characteristic color of interstitial cells, and hence, the color of these tumors Microscopically these tumors are unlike any other testicular neoplasm "The liver-like cells, with round to slightly oval nuclei and eccentric punctate nucleoli are without a counterpart "

That the interstitial cells of Leydig produce the androgen excretion responsible for the male characteristics such as enlargement of the penis, distribution of the facial and body hair in the male pattern and deepening of the voice is generally accepted The same testosterone also induces the enlargement of the prostate and seminal vesicles and promotes the secretory action of these organs It is also a factor, directly or indirectly, in the closure of the epiphyseal lines with the resultant stunting of growth and, in these cases, the marked muscular development

Even though these changes which have occurred are in the transitional process, the testis or testes, as in this case, in the absence of activation by pituitary gonadotrophins remain infantile As Silagy has said, "this situation constitutes sexual maturation of the incomplete variety "

The 17-ketosteroids of testicular origin are known to be metabolites of androgen secretion by the interstitial cells but the urinary secretion of 17-ketosteroids is not dependent on the activity of the testes alone since the adrenal cortex is also an important source Since the alpha portion is thought to come from the interstitial cells and the beta from the activity of the adrenal cortex, the relative proportion of these two components must be determined It appears advisable, therefore, to examine the urine for the alpha and beta portions Some believe the urinary excretion of estrogens is a more accurate and reliable indication of interstitial cell function than 17-ketosteroid determinations since the estrogens in males are mainly testicular in origin Staubitz et al say, "The adrenal cortex is presumed to be the sole source of dehydroisoandrosterone, one of the members of the beta fraction The change in the quantitative excretion of dehydroisoandrosterone and the resulting change in the beta fraction are therefore generally indicative of adrenal cortical malfunction "

The case reported by Staubitz et al had a marked increase of 17-ketosteroids postoperatively with a gradual decline There was no satisfactory explanation for this phenomenon Masson and Venning's case showed that "the 17-ketosteroid level elevated fifty times above the normal mean in a 24-hour urine specimen Three determinations made in the presence of metastases one to two months before death were elevated at 980, 1035 and 1040 milligrams per day These are the highest ever recorded including those of adrenal tumors The serum 17-ketosteroid level was 16 mg per cent " See table 2

Talbot et al have determined the normal excretion of 17-ketosteroids for normal and abnormal children They found no significant difference between boys and girls up to 18 years of age, and also noted a gradual increase from the age of 5 up to 12 when the excretion was 0 to 1 mg , until 18 years when it ranged from 4 to 11 mg per day The average for adult women was 6 8 mg and for men 11 0 mg "Children who have reached their twelfth birthday should excrete at least 1 0 milligram of 17-ketosteroids daily " See table 2

The figures taken from Kenigsberg, Pearson and McGavack are indicated in table 2 which shows a normal of 9 4 in a male from 13 to 16 years of age (This case had 19 0 mg 30 months postoperatively) They believed that the average

TABLE 2 *17 Ketosteroids average daily excretion**

	yrs	mg
Children	0–5	1 4
	5–12	3 8
Males adult	13–16	9 4
	17–34	18 0
	35–49	15 0
	50–75	9 0
Females adult		9 3

* The average varies by not more than 2 0 mg

(Taken from Kenigsberg Pearson & McGavack J Clin Endocrin , 9 426, May 1949) varies by not more than 2 mg from the mean In view of the normal findings listed in table 2 the case herewith presented should have daily excretions of 9 4 mg according to his present age The repeated observations for almost 3 years have failed to indicate any additional reason to suspect that another tumor is present

These cases apparently go on in a relatively normal manner, the great difference, of course, being that they have matured prematurely Where the tumor has been removed in the early stages of the disease there appears to have been some regression of the secondary sex characteristics Reports on the bone development have not been made so it is not known whether additional growth has taken place in the cases reported Where the epiphyseal lines have closed it is unlikely that additional growth will take place and this is likely to be so in this case which had gone for years before removal of the tumor Several authors have reported the siring of children by their patients prior to the finding of the tumor but no report indicates the birth of children after the removal of the tumor Some of the younger ones who have had unilateral tumors should be reported upon later regarding the possibility of sterility of the opposite testis

These tumors are most likely to be confused with arrhenoblastoma, adrenal cortical rests and Sertoli cell tumors In all cases suspected of interstitial cell tumors the preoperative studies upon the excretion of estrogens, androgens, 17-ketosteroids, gonadotrophins, and such intermediary products as pregnandial should be carried out

CONCLUSIONS

A case of interstitial cell tumor found outside the testis is herewith reported It is the second known case to have been found outside the testis and had been present for at least 7½ years before removal Metastases, the only positive evidence of malignancy, have not yet developed

Since this paper was presented, another case of bilateral interstitial cell tumor of the testicle has been reported by Doctors Rezek and Hardin in the Journal of Urology (vol 74, pp 628–635, November 1955)

The author acknowledges his indebtedness to Drs E Clyde Krug and Richard McManus and Mr Jack Vetter for their aid in the study of this case

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FEMALE PSEUDOHERMAPHRODITISM A CASE PRESENTING UNUSUAL PROBLEMS

JOHN E GLEN

X , a 24-year-old white married man was referred to the office on July 13, 1951 with the complaint of tenderness in the right lower abdomen accentuated upon physical exertion and noticed for approximately one year He also noticed swelling of the right lower abdomen at a previous operative site for approximately four months A low lumbar backache had been present for about two months, noticed mostly when resting and relieved on motion The patient stated that he had a congenital penile deformity and believed that his left testicle had been removed at a previous operation He stated that the penis curved ventrally on erection There were no urinary complaints except an occasional burning on voiding Nocturia was zero to one time and the patient voided five to six times during the day There was no history of hematuria or passage of urinary calculi

The patient was found to be of small stature, weighing 128 pounds and approximately 5 feet, 2 inches The beard was sparse, mostly on the chin There was very little hair present on the chest and about the nipples Examination of the abdomen disclosed a soft, tender, somewhat movable mass, lateral to the right rectus muscle and 5 cm above the pubic symphysis A broad suprapubic midline scar was present A marked chordee with penoscrotal hypospadias was found There was no evidence of abdominal hernias Rectal examination disclosed a small, tender prostate gland Voided urine showed no sugar or albumin, 3 to 5 white cells per high powered field were present and the pH was 5 5 There was not sufficient specimen for a specific gravity determination

The patient was placed on mandelamine and was seen one week later At that time, the urine specimen showed only an occasional white cell and a specific gravity of 1 020 The pH was 7 5 and no sugar or albumin was found

In view of the pain and swelling complained of, the patient was hospitalized with a tentative diagnosis of neoplasm of the remaining testicle which had been intra-abdominal for many years The patient was admitted to the Ellis Hospital, Schenectady, N Y on July 24, 1951, and the following day biopsy of the right gonad was obtained At operation, an incision was made through the skin and subcutaneous tissue overlying the area of swelling and tenderness A firm whitish organ was easily identified and appeared to be an ovary There were several small cystic areas present containing clear and somewhat brownish bloody fluid Biopsies were taken from three sites Hemostasis was easily obtained with fine atraumatic catgut sutures The skin was closed with black silk sutures The report of the biopsy showed 'Ovarian tissue showing abundant stroma and a few immature and maturing ova The capsule is quite thick No inflammatory or neoplastic change Other fragments show distinct follicle cysts "

An additional laboratory study of 17-ketosteroids was undertaken and the report was 'Received 1470 cc urine for 24-hour specimen, 3 8 mg 17-ketosteroids

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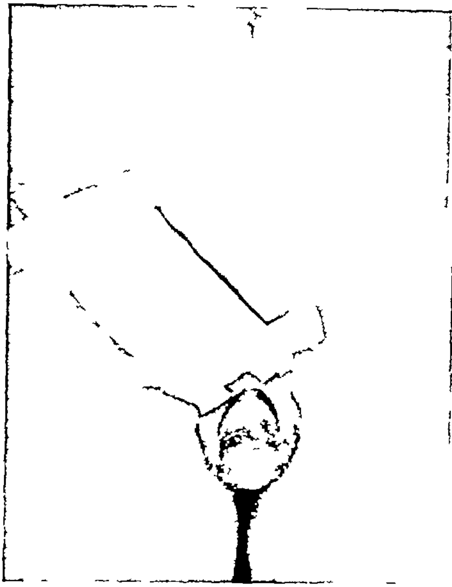

FIG 1

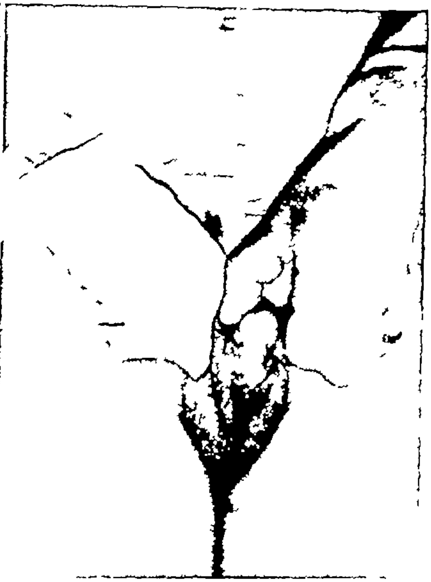

FIG 2

in 24 hours Normal for men, 7–27 mg per 24 hours " The routine laboratory studies were not remarkable

The patient had an easy postoperative course and was discharged on July 29, 1951 During the stay in the hospital the accompanying photographs (fig 1) were taken

The patient was seen in the office over a period of 16 months He had no further complaints of pain or tenderness About fourteen months after operation he became concerned about the inability of his wife to conceive He stated that he felt there was some loss of sexual desire, and intercourse was reduced from four or five times per week, to once a week since operation He stated that ejaculation occurred and consisted only of a few drops of fluid which he was unable to collect for examination He also stated that for approximately six months he noticed an increase in hair growth on his chest and about the nipples and shaved every one and a half to two days He also inquired as to the advisability of surgery for correction of his genital deformity with straightening of the chordee and repair of the hypospadias The patient was not encouraged to have this done

Past history Review of the past history of this patient disclosed three previous hospital admissions On the first occasion, the patient was admitted on September 21, 1944 and discharged on September 28, 1944 The final diagnosis was bilateral abdominal ectopic testes and hypospadias The patient underwent right orchiopexy with fixation to the pubic symphysis The patient at operation was thought on palpation to have the internal organs of an apparently normal male but with extremely short spermatic cords The right testicle was delivered from the abdomen with considerable difficulty due to the shortening The testicle was sutured to the periosteum of the symphysis with a chromic suture through the gubernaculum The postoperative course was uneventful

The patient was readmitted to the hospital for the second time on November 9, 1944 and discharged on November 20, 1944 with a final diagnosis of pseudohermaphroditism At operation, the gonad, previously thought to be a left testicle and epididymis, was found to be a tube and ovary This was removed and palpation of the area posterior to the bladder disclosed a firm enlargement which was thought to be a probable rudimentary uterus The bladder was distended with water and a suprapubic cystotomy was done The gonad, previously operated upon and considered to be a right testicle, was found on palpation to be fixed to the upper border of the pubic symphysis The specimen submitted to the laboratory showed the following results "Biopsy left (testicle) (tissue?) Specimen consists of six pieces of grayish tissue which are identified as follows One piece, the largest, measures 3 5 by 3 by 1 5 cm It has a partially smooth outer surface and when sectioned closely simulates an ovary in which there is a cortex containing small cysts filled with clear fluid, one of these cysts measures 0 5 cm in diameter The medullary portion is grayish-white and fibrous and also contains a cyst 0 4 cm in diameter filled with brownish clot Another piece of tissue is 5 cm long and 0 6 cm in diameter It is cylindric with outer smooth, grayish-brown surfaces At one end are structures suggesting fimbriae The other four pieces are nondescript grayish fragments with brownish blood clot attached and which resemble ovarian tissue Fallopian tube Early acute inflammation Numerous polynuclears on the serosa and surrounding blood vessels Ovary Small follicular cysts, otherwise normal Many ova in cortex Fragments of ovarian tissue Normal"

The postoperative course was again uneventful and the patient was discharged in good condition with a cystotomy tube in place

He was readmitted to the hospital for the third time on January 20, 1945 and was discharged January 22, 1945 with the same diagnosis of pseudohermaphroditism A cystoscopy was done under general anesthesia which disclosed a normal bladder Observation of the posterior urethra was done to determine the presence of any abnormalities which could not be found or located The cystotomy tube was removed and the patient again discharged in good condition

Family history Further study of the family history was made and proved to be most interesting It was found that this entire family had been studied from a genetic standpoint by the late Dr Judson B Gilbert of Schenectady, New York and Dr James Hamilton of Long Island, New York and reported verbally at a meeting in Chicago This study, to the best of my knowledge, never appeared in print The mother and father were alive and well, as were seven children Three of the children presented obvious external genital abnormalities The other five were normal females One member of this family died during an exploratory laparotomy The cause of death was not determined The only common factor found in this entire family appeared to be that of short stature

In considering this case several very important factors are brought to mind In the opinion of the writer it would hardly seem justifiable to inform the patient of the establishment beyond doubt of the sex being that of a female The patient has lived his entire life as a male and is gainfully employed as a chauffeur He has married and is apparently living a satisfactory sexual life One of his great regrets, and that of his wife's is their inability to produce children His wife has made several visits to a gynecologist because of the existing sterility problem After a time, the wife made it clear that she understood she would never become pregnant and was apparently content to drop the entire matter

The gynecologist who had referred the patient originally was consulted and concurred with the writer that an explanation to the patient of his condition might well result in possible drastic action even to the point of self destruction He and the writer also felt that such a disclosure might well result in the disruption of a marital relationship In addition, the opinion of three other urologists was obtained It was the feeling of all three that the interests of the patient might best be served by not informing him of the findings It was not considered advisable to discuss this matter with the patient's parents as they are quite aged and have a marked language barrier Consequently, at the time of the writing of this paper, no attempt has been made to discuss the situation with either the patient or his parents

CONCLUSION AND SUMMARY

An interesting case history is presented in which it has been found that a happy marriage is existing between a female pseudohermaphrodite and a normal female

In view of the above findings, it would seem that the disclosure of the details of this case to the patient would obviously be disastrous to the lives of a couple who are enjoying a happy and normal marriage

The author wishes to thank Dr T Admolfi and Miss Eilleen Doyle of Schenectady, New York for making the presentation of this case possible

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THE NERVOUS SYSTEM AS RELATED TO FERTILITY AND STERILITY

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A vast literature has accumulated wherein much information is compiled and correlated describing the relationships between the male sex organs and the endocrines. Likewise numerous descriptions are available relating the effects of nutrition, infections, and trauma, upon the various segments of the male reproductive system. It is well recognized that the proper function of the male genitalia is dependent upon an intact and normal nervous system. There appears, however, to be a need for assembling the scattered information of the neurogenital physiology to afford a clearer concept of the normal and abnormal behavior of the components of the male reproductive system.

The knowledge of the neurogenital function has been largely accumulated by 1) anatomical dissections, 2) experimental studies on laboratory animals, particularly the cat, 3) by observation of patients with lesions of the central nervous system and spinal cord, and 4) undesired consequences from surgical operations. The fertility of the individual may be adversely affected by disorders of the nervous system either by 1) incapacity to perform the sexual act, or 2) direct alterations in the reproductive organ themselves, or both. The following schema may assist clinical orientation by outlining some of the neurological lesions that affect the male genitalia.

1. Congenital defects
   Example—Spina bifida
2. Postinflammatory lesions
   Example—Tabes dorsalis
3. Degenerative lesions
   Example—Parkinsonism
4. Focal lesions
   a) Partial or complete cord injuries
      Example—Paraplegia
   b) Injury to the lumbar and pelvic nerves
      Example—Postsympathectomy
5. Psycho-sexual aberrations
   Example—Functional impotence

The capacity of man to consummate coitus involves numerous nervous mechanisms and pathways. Excitation and the performance of the sexual act is an extremely complicated neurologic activity, involving the special sense organs, the brain, the spinal cord, and the afferent and efferent nerve pathways to and from

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the genitalia The nervous anatomical variations in the human sympathetic systems and atypical arrangements of paravertebral ganglia, with cross axones, have introduced a variety of responses that account for some inconsistencies of function With deference to these variations and lack of precise knowledge, and at the risk of over-simplification, it is of advantage to analyze the sex acts as having four components subject to neurologic domination These are 1) erection, 2) emission, 3) ejaculation and 4) detumesence

1 ERECTION

Erection may be provoked by 1) intense sexual excitement in the higher centers, or 2) by local stimulation of the glans penis, or 3) as a sacral reflex arc

The tumefaction of the penis is accounted for by the distention of the three corpora with blood These cylindrical erectile masses are surrounded by fibrous tissue which in turn are encased by the perineal musculature Blood reaches the corpus by way of the internal pudendal arteries, and by a pair of dorsal arteries lying on the superior side of the penis The cavernous artery runs longitudinally in each corpus cavernosum furnishing blood to the irregular vascular erectile spaces interposed between arteries and the veins Upon dilatation of the artery the blood flows into the spaces in enormously increased amounts reaching pressures approximating that in the carotid artery [1] The mechanism by which blood is partially trapped in the erectile tissue is still in dispute The large veins are thought by some to have funnel-like valves which impede the return This may be associated by pressure against the tunica surrounding the corpora There is little, if any, cross arterial communication between the corpus as indicated by the observations of Henderson and Roepke, who injected methylene blue into the artery supplying one corpus without seeing blue in the other corpus until a pressure of 200 mm of mercury was reached [2] These observers discredit the assumption that the perineal muscles surrounding the penis accounted for retention of blood in the corpus by compression May and Hirtl have demonstrated that radiopaque contrast media injected into one corpus cavernosum will fill both corpora and visualize the efferent veins leaving the penis [3] The accompanying cavernograms, taken by ourselves, illustrate this venous communication and venous system draining the blood into the pelvic vessels (fig 1)

The control of the arterial venous action is supervised by nerve impulses (fig 2) Psychic stimulation will produce an erection but such will also take place purely as a result of a sacral reflex arc involving S-2, S-3, and S-4 Electric stimulation of S-1 causes quick protusion of the penis in the cat [4] Excitation of S-2 completes the erection and S-3 causes arterial dilatation and passive decrease in venous outflow These efferent impulses leave the spinal cord from the anterior division of S-2, S-3 and S-4 and course through the pelvic nerve (hence, it re-

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[1] Fulton, J F A Textbook of Physiology Philadelphia W B Saunders Co , 1955, p 1275

[2] Henderson, V E and Roepke, M H Am J Physiol , **106** 441–448, 1933

[3] May, F and Hirtl, H *Urologica Internat* , **1** 120–134, 1955

[4] Semans, J H and Langworthy, O R J Urol , **40** 836–846, 1938

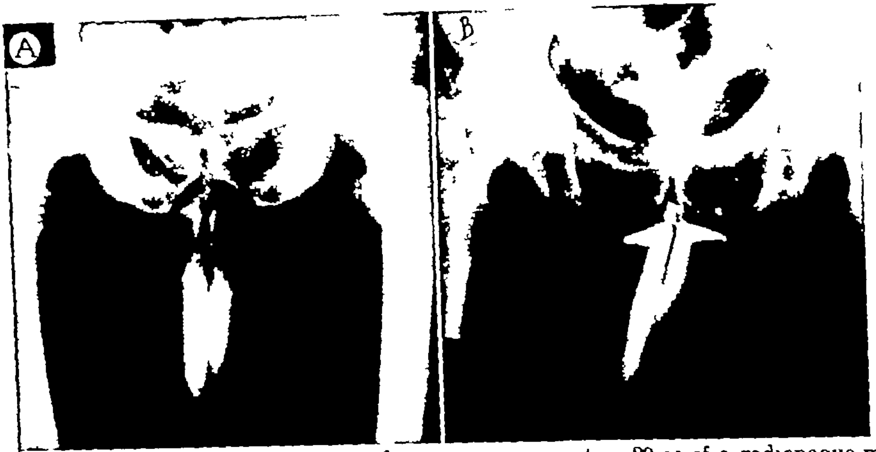

FIG 1 *A*, anterior-posterior views of cavernogram injecting 20 cc of a radiopaque medium, with a No 20 gage needle at pressure of 25 mm of mercury *B*, anterior-posterior view of cavernogram

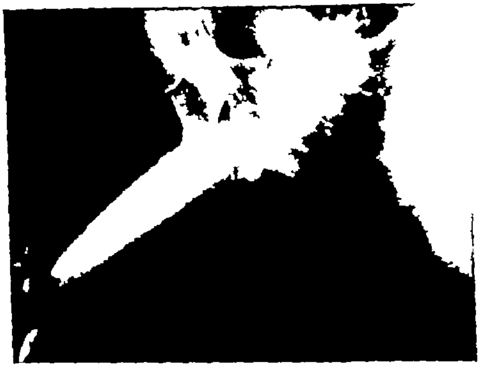

FIG 2 Lateral view of cavernogram (same as fig 1, *B*)

ceives it name nervus erigans), and pudendal nerves The pelvic nerve carries parasympathetic impulses responsible for active dilatation of the arteries of the penis, while the pudendal nerve carries impulses which cause contraction of the bulbo- and ischiocavernosus muscles, thus decreasing the venous outflow from the penis Sensory receptors in the skin of the penis send afferent impulses over the pudendal nerve to complete the reflex arc

Whereas it is evident that the nerve impulses leading to the erection are essentially parasympathetic in type, there are probably elements of central or sympathetic control The latter is evidenced by the fact that 57 per cent of patients who have had sympathectomies at levels as high as T-1 or T-2 have loss of the power of erection [5] A continuous flow of blood is necessary to maintain the erection for it has been shown that mechanical constriction of the aorta produces flaccidity despite continued and strong electrical stimulation [4]

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[5] Whitelaw G P and Smithwick R H New Eng J Med 245 121–130, 1951

2 EMISSION

The special sense organs of the glans penis are activated by friction and send afferent impulses over the internal pudendal nerve to the spinal cord Efferent impulses then leave the upper lumbar segments (L-2, L-3) which travel over the lumbar rami communicantes and the hypogastric nerves, through the hypogastric plexus to the presacral nerve in the human The epididymides and the proximal vasa receive fibers from the hypogastric plexus (sympathetic), whereas the distal portion of the vasa probably are innervated by fibers from the vesical plexus, containing fibers from both sympathetic and parasympathetic systems Therefore, the musculature of the epididymides, vasa and prostate is largely controlled by *the sympathetic system The smooth muscles contract under stimuli* traveling through the above described pathways and the combined prostatovesicular secretions flow into the posterior urethra producing the emission Learmouth stimulated the presacral nerve and observed these fluids pouring into the urethra [6] Simeone denervated the ductus deferens and, although complete *paralysis did not follow, there was interference with peristalsis* [7] Presacral neurectomy or bilateral lumbar sympathectomy to include L-1, L-2, L-3 causes loss of erection or ejaculation or both [8]

3 EJACULATION

Ejaculation is thought to be purely a reflex action Emission of semen into the prostatic urethra is the trigger-impulse which elicits afferent impulses by way of the pudendal nerve to S-2, S-3, and S-4 and return as efferent impulses to the perineal muscles Contraction of the bulbocavernosa, ischiocavernosa and other pelvic and perineal muscles accounts for the expulsion of semen from the urethra The internal and external sphincter play a part in the ejaculation, the explanation being that the internal sphincter contracts by way of the sympathetic fibers preventing retrograde ejaculations, and the external sphincter, innervated by the fibers of the pudendal nerve, opens to permit the semen to escape See figure 3

4 DETUMESENCE

The efflux of blood from the cavernous spaces in the penis is due to arterial constriction which clearly has its center of innervation in the sympathetic system Detumesence follows the ejaculatory action Electric stimulation of the sympathetic nerve sends impulses via the hypogastric and presacral nerves to cause arterioconstriction and vasodilatation

It is thus appreciated that the act of sexual excitement, erection, ejaculation and emission is a complicated, sequential and co-ordinated action A discordancy in any, or all, of these components is capable of partially or completely disrupting the ability for normal consummation of coitus A variety of disabilities are appreciated by study of patients with cord lesions, lumbodorsal sympathectomies, and patients who complain of impotence Erections may be provoked

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[6] Learmonth J B Brain, 54 147, 1931

[7] Simeone, F A Am J Physiol, 103 582–591, 1933

[8] Detakats G and Helfrich L S J A M A 117 20–21, 1941

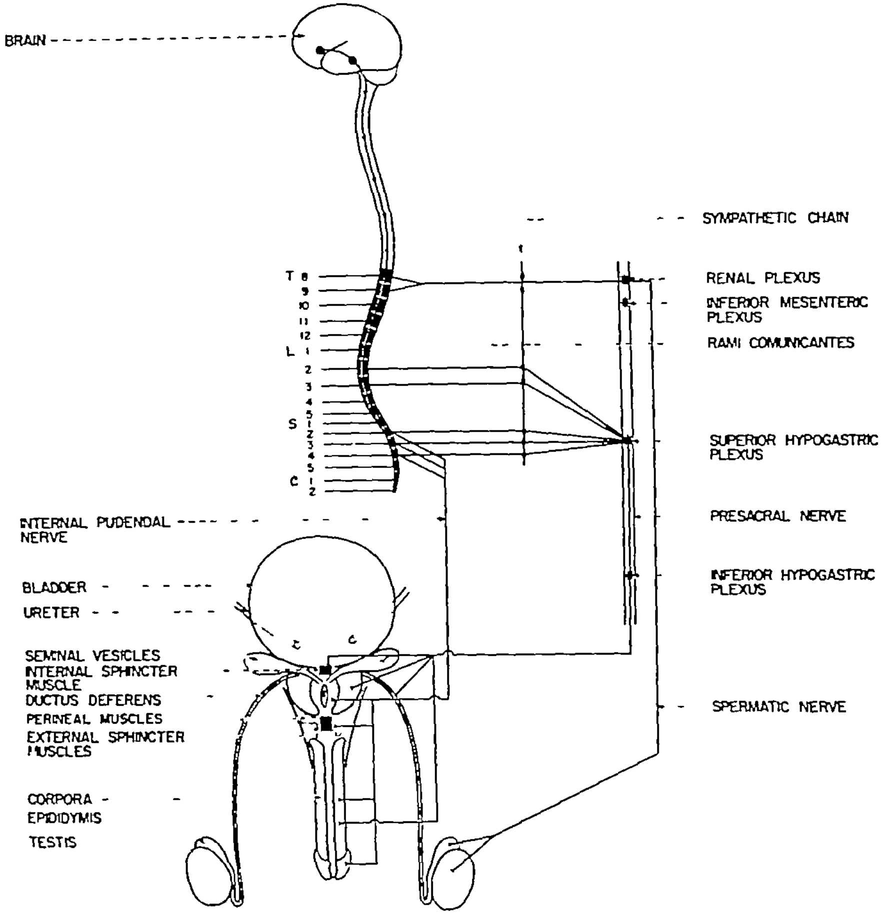

FIG 3 Schematic representation showing the innervation of the reproductive system

and coitus may be performed without sensation and without ejaculation Semen may be deposited in the bladder and not escape from the urethra Premature ejaculation takes place without erection Talbot studied 200 paraplegics and divided them into three groups[9] Thirty-six per cent never had an erection since the onset of the cord lesion, 42 per cent experienced erection only with local stimuli, and in 21 per cent erections could be induced by local or psychic stimuli In summary 46 of 200 were able to have intercourse, but only 20 of 200 were able to achieve intromission and ejaculation

Attempts have been made with paraplegic patients to incite emission and ejaculation by electrical currents applied to the verumontanum through insulated sounds[10] The quality of such seminal specimens is poor and the results discouraging Intrathecal injections of 0 2 to 0 5 mg prostigmine in 1 1000 aqueous solutions injected at L-4 and L-5 are reported to be followed in 1 hour by erection

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[9] Talbot H S J Urol **61** 265–270, 1949

[10] Horne, H W Jr, Paull, D P and Munro, D New Eng J Med **239** 959–961, 1948

2 EMISSION

The special sense organs of the glans penis are activated by friction and send afferent impulses over the internal pudendal nerve to the spinal cord Efferent impulses then leave the upper lumbar segments (L-2, L-3) which travel over the lumbar *rami communicantes and the hypogastric nerves, through the hypogastric* plexus to the presacral nerve in the human The epididymides and the proximal vasa receive fibers from the hypogastric plexus (sympathetic), whereas the distal portion of the vasa probably are innervated by fibers from the vesical plexus, containing fibers from both sympathetic and parasympathetic systems Therefore, the musculature of the epididymides, vasa and prostate is largely controlled by the sympathetic system The smooth muscles contract under stimuli traveling through the above described pathways and the combined prostatovesicular secretions flow into the posterior urethra producing the emission Learmouth stimulated the presacral nerve and observed these fluids pouring into the urethra [6] Simeone denervated the ductus deferens and, although complete paralysis did not follow, there was interference with peristalsis [7] Presacral neurectomy or bilateral lumbar sympathectomy to include L-1, L-2, L-3 causes loss of erection or ejaculation or both [8]

3 EJACULATION

Ejaculation is thought to be purely a reflex action Emission of semen into the prostatic urethra is the trigger-impulse which elicits afferent impulses by way of the pudendal nerve to S-2, S-3, and S-4 and return as efferent impulses to the perineal muscles Contraction of the bulbocavernosa, ischiocavernosa and other pelvic and perineal *muscles accounts for the expulsion of semen from the* urethra The internal and external sphincter play a part in the ejaculation, the explanation being that the internal sphincter contracts by way of the sympathetic fibers preventing retrograde ejaculations, and the external sphincter, innervated by the fibers of the pudendal nerve, opens to permit the semen to escape See *figure* 3

4 DETUMESENCE

The efflux of blood from the cavernous spaces in the penis is due to arterial constriction which clearly has its center of innervation in the sympathetic system Detumesence follows the ejaculatory action Electric stimulation of the sympathetic nerve sends impulses via the hypogastric and presacral nerves to cause arterioconstriction and vasodilatation

It is thus appreciated that the act of sexual excitement, erection, ejaculation and emission is a complicated, sequential and co-ordinated action A discordancy in any, or all, of these components is capable of partially or completely disrupting the ability for normal consummation of coitus A variety of disabilities are appreciated by study of patients with cord lesions, lumbodorsal sympathectomies, and patients who *complain of impotence Erections may* be provoked

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[6] Learmonth, J B Brain, 54 147, 1931

[7] Simeone, F A Am J Physiol, 103 582-591, 1933

[8] Detakats, G and Helfrich, L S J A M A, *117 20-21, 1941*

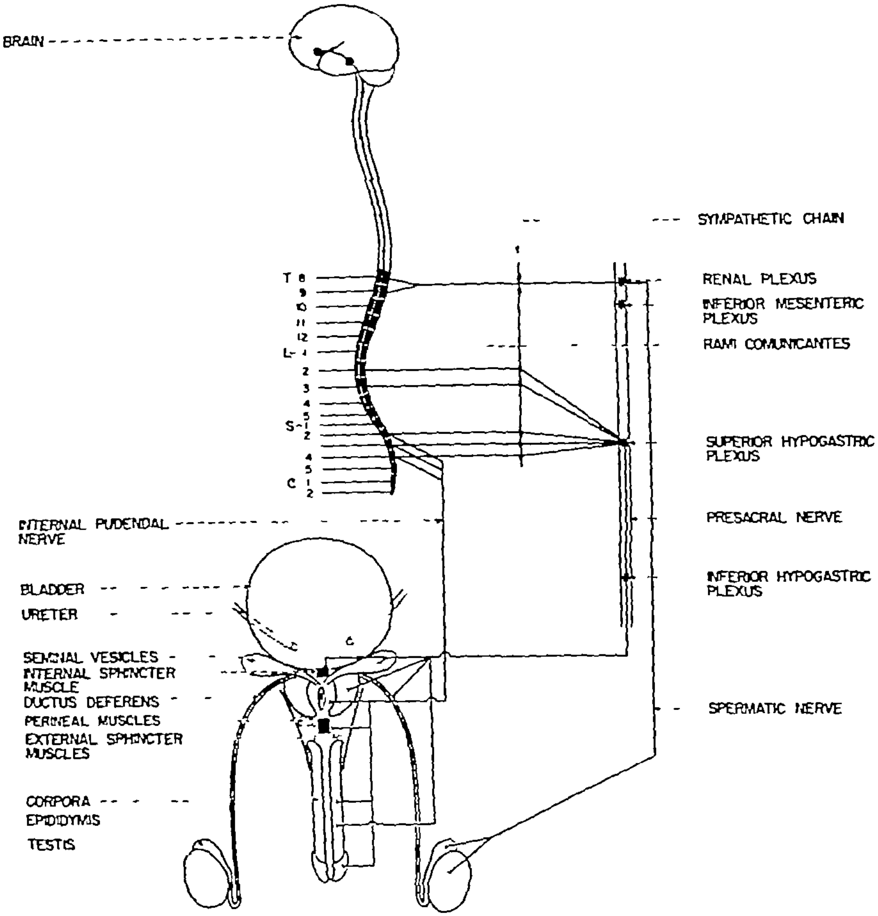

Fig 3 Schematic representation showing the innervation of the reproductive system

and coitus may be performed without sensation and without ejaculation Semen may be deposited in the bladder and not escape from the urethra Premature ejaculation takes place without erection Talbot studied 200 paraplegics and divided them into three groups[9] Thirty-six per cent never had an erection since the onset of the cord lesion, 42 per cent experienced erection only with local stimuli, and in 21 per cent erections could be induced by local or psychic stimuli In summary 46 of 200 were able to have intercourse, but only 20 of 200 were able to achieve intromission and ejaculation

Attempts have been made with paraplegic patients to incite emission and ejaculation by electrical currents applied to the verumontanum through insulated sounds[10] The quality of such seminal specimens is poor and the results discouraging Intrathecal injections of 0 2 to 0 5 mg prostigmine in 1 1000 aqueous solutions injected at L-4 and L-5 are reported to be followed in 1 hour by erection and ejaculation Guttman used semen so obtained for artificial insemination without results[11] Spira, however, recovered seminal specimens and succeeded in impregnating the wife of a totally incapacitated man[12] Most of the specimens were poor but on one occasion he reported securing semen with a cell count of two hundred million having 50 per cent motility

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[9] Talbot H S J Urol 61 265-270, 1949
[10] Horne, H W Jr, Paull, D P and Munro, D New Eng J Med, 239 959-961, 1948

The testes themselves suffer cytological damage as a consequence of injury to the nerve supply The testes are supplied by sympathetic fibers arising from indefinite levels in the cord, possibly at T-10 and T-11 or higher After synapse with the sympathetic chain ganglia these fibers pass to the renal ganglia and emerge as the spermatic nerves descending to the testes along the spermatic arteries[13] [14] The spermatic nerves probably assist in the thermo-regulatory mechanism for they control the caliber of the arteries and possibly of the veins of the testicular vessels, thereby regulating blood flow and heat dispersion There is no evidence of a nerve supply to the epithelium of the tubules or the interstitial cells Destruction of this nerve has resulted, however, in atrophic changes in the germinal epithelium and hypertrophy of the interstitial tissue[15]

A number of investigators have secured testicular biopsies from men with partial and complete cord lesions[16] [17] All report that moderate to advanced deterioration of spermatogenesis was found in the majority of paraplegic men Bors and his associates also studied, concomitantly, the circulating androgens, estrogens, and pituitary hormones The 17-ketosteroids were elevated in 9 of 34 patients In the same group estrogens were increased in 30 and the pituitary gonadotrophins were low in 25 patients[13]

A variety of factors must be considered to account for the disruption of spermatogenesis in men with cord lesions Thermo-regularity control is altered by paralysis of the cremasteric reflex, loss of normal sweating of the scrotum and arterial dilatation of testicular vessels Depressant effects of excessive androgens and estrogens may be a factor inhibiting spermatogenesis Infection and nutritional deficiency are also unfavorable influences

The future will doubtless provide numerous opportunities to revise many of the statements contained herein, as new observations and discovery revise our knowledge A prediction is ventured, however, that the importance of neurological influence over the reproductive system will be emphasized, rather than minimized, in the years to come

[11] Guttman, L Fourth Neurologic Institutional Conference, vol 2, p 69, 1949

[12] Spira, R Lancet, **1** 670–671, 1956

[13] Rosenquist, R C , Bors, E , Engle, E T and Holliger, M D J Clin Endocrinol, **10** 381–397, 1950

[14] Kuntz, A J Comp Neurol , **85** 33–44, 1946

[15] Kuntz, A Anat Rec , **17** 203–219, 1919

[16] Klein, M M , Fontaine, R , Davy, A and Frank, P Revue Neurologique, **36** 501–503, 1952

[17] Stemmermann, G N , Weiss, L , Auerbach, O and Friedman, M Am J Clin Path , **20** 24–34, 1950

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THE EFFECT OF TESTOSTERONE ON THE AZOTEMIC PATIENT*

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The urologist is so frequently confronted with the problem of the azotemic patient that he constantly searches for a rational and effective solution We are presenting a preliminary report of the clinical and chemical results of androgen therapy for chronic uremia and acute exacerbations of patients in chronic uremia —both groups being of the nonobstructive type The rationale of this effective approach is presented We hope that other urologists may try and clinically evaluate this therapy

Prevost and Dumas[1] first noted in 1821 that urea accumulates in the blood of an animal following the removal of both kidneys Subsequent to this, many of the clinical features of renal insufficiency were accurately traced to nitrogen retention Autopsy on uremic patients reveals many organic changes in the nervous system such as sclerosis of cerebral vessels, accumulation of urea in the cerebral cortex and edema of the brain [2] Well known is the almost universal symptomatology of azotemia with its lethargy, headaches, weakness and respiratory and gastrointestinal symptoms These are the plague of the patient and physician

We have attempted to take advantage of the anticatabolic properties of androgen to aid the damaged kidney to better compensate for its azotemic load Although we think of uremia as "nitrogen retention," it may be more accurately described as renal decompensation That is, the kidneys are unable to handle the amount of nitrogen waste presented to them It is at this point that we try to aid the patient with failing kidneys by enabling him to be in nitrogen balance by reason of having less tissue breakdown As a result, his nitrogen intake may be less and his nitrogen excretion consequently smaller

Recent experiments with amino acids tagged with heavy hydrogen reveal that amino acids from protein intake go into a common pool [3] There is a continuous exchange between the amino acids of this pool and those of the breakdown of tissue protein Therefore, by decreasing tissue breakdown, the nitrogenous excretory load to the damaged kidneys can also be decreased Addis[4] working with healthy medical students showed that the blood urea nitrogen level was directly related to the protein intake For example, a patient with chronic uremia and av-

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Read at annual meeting, North Central Section of American Urological Association, Cleveland, Ohio, October 3–5, 1956

Depo testosterone (cyclopentylpropionate) was supplied by the Upjohn Company, Kalamazoo, Mich

* Further investigation of this work is being supported by a grant from the Dr Jerome D Solomon Memorial Research Foundation

† Dr Jerome D Solomon Research Fellow at the Cook County Hospital in Chicago

[1] Ann de Chim et Phys , 23 (second series) 90, 1821

[2] J of Nerv and Mental Dis , 120 303–315, 1954

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[4] Fishberg A M Hypertension and Nephritis Philadelphia Lea and Febiger, 1954, p 57

erage urea clearance of 6 cc per minute, who is excreting 2 cc urine per minute and requiring the excretion of 5 0 gm of urea nitrogen per day, would have a blood urea nitrogen of 58 mg per 100 cc

$$C_{urea} = \frac{U}{B} \times V$$

However, with the aid of the anticatabolic effect of androgen therapy this same patient may be able to achieve nitrogen equilibrium with the excretion of 4 0 gm protein nitrogen per day and a subsequent reduction of his blood urea nitrogen to 46 mg per 100 cc This hormonal "crutch" may be the difference between marked azotemic symptoms and a clinically improved, satisfied patient

Long acting testosterone (cyclopentylpropionate) in oil 50 mg intramuscularly daily was administered these patients, in conjunction with a low protein, high carbohydrate and high fat diet This therapy was used on 16 patients four with polycystic kidneys, seven with primary nephritides and five with malignant or benign nephrosclerosis Maintenance dose was 100 mg weekly

It is our hope to present a complete and detailed progress report of all the patients treated by this regimen after at least a year of study In this preliminary report of a 6-month period, several representative cases follow

CASE REPORTS

Case 1 Mr W H , aged 44, had had known bilateral polycystic disease for 10 years He was admitted to the hospital May 23, 1956 because of hematuria The admission nonprotein nitrogen was 57 5 ml and the creatinine 2 78 mg A daily dose of 50 mg of testosterone propionate was administered intramuscularly and the low protein, high carbohydrate and high fat diet instituted Six days later the nonprotein nitrogen was 39 5 mg and the creatinine 2 15 mg Twelve days after admission, the urine became clear and the nonprotein nitrogen and creatinine had stabilized at 39 5 mg and 1 75 mg respectively Since discharge the patient has been receiving 100 mg testosterone once weekly and the blood chemistry levels have remained essentially the same The patient states that he feels better than he has in years and has resumed his work and sports activities, including golf

Case 2 Miss M M E , aged 33, had bilateral polycystic disease for 5 years Her mother and sister died of the disease During the past year she was hospitalized 4 times because of nausea, vomiting and headaches accompanying marked episodes of azotemia The first 3 times, a response to androgen therapy produced a decline in nonprotein nitrogen from levels above 170 mg to below 90 mg Finally on her last admission, the azotemia was accompanied by cardiac failure and she expired

It is believed that androgen therapy made the patient more comfortable and able to work between the episodes of marked azotemia requiring hospitalization

Case 3 Mr F A B , aged 36 years, was a known azotemic for 16 years, the diagnosis was benign nephrosclerosis His blood pressure on admission to the hospital March 22, 1956 was 170/90 Urea clearance was 8 4 cc or 15 5 per cent The nonprotein nitrogen was 107 5 mg and the creatinine 5 75 mg Androgen therapy was instituted After 8 days of 50 mg testosterone daily, the nonprotein nitrogen declined to 76 5 mg and the creatinine to 3 15 mg Since discharge, maintenance therapy has been 100 mg weekly and the blood chemistry values have remained essentially the same There has been no decrease in the blood pressure At the present time the patient is doing heavy labor in a section gang for the street car company and working every day

DISCUSSION

In spite of the clinical effectiveness of this therapy, we had some hesitance because of the fear of activating a latent carcinoma of the prostate in a man in the older age group However, in a well controlled clinical experiment by investigators, it was found that "there was no evidence that testosterone propionate had initiated or activated latent carcinoma of the prostate "[5] In evaluating therapy in women, the problem of untoward masculinizing effect must be considered Androgen therapy was used in treating women with psychoses It was found that neither young nor old women demonstrated virilizing changes from androgen therapy[6] Several women patients in our group experienced marked increase in their libido

SUMMARY

Utilization of the anticatabolic properties of androgen has been demonstrated in the azotemic patient Several representative cases have been presented and the possible modes of action of androgen in uremia are suggested We present this only as a preliminary report A future detailed report is planned on the application of androgen therapy in the azotemic patients with urinary retention compared with patients who have primary kidney disease This future report will also include blood level studies of sodium, potassium and calcium in an effort to follow their course during androgen therapy and evaluate their possible role in a favorable response

30 N Michigan Ave , Chicago , Ill

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[5] Lesser, Maurice A , et al Effect of testosterone propionate on the prostate gland of patients over 45 J Clin Endocrinol and Metabol , 15 297, 1955

[6] S Cosyns-Durat Presse méd , 64 231, 1956

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EXFOLIATIVE CYTOLOGY OF THE URINE WITH SPECIAL REFERENCE TO NEOPLASMS OF THE URINARY TRACT PRELIMINARY REPORT

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From the Department of Pathology, The Cleveland Clinic Foundation, and The Frank E Bunts Educational Institute, Cleveland, Ohio

Although the urine was one of the sites where neoplastic fragments were first identified,[1] it was not until 1947 that cytologic examination of the urinary sediment was reported to be of value in revealing tumor of the urinary tract[2a, b] This finding was supported by the reports of Chute and Williams[3] and Fremont-Smith, Graham and Meigs[4] Since these earlier studies,however, there have been relatively few reports and not all have been enthusiastic[5] Technical difficulties have been encountered as a result of unsatisfactory smears[3]—22 2 per cent were unsatisfactory in a recently reported series[6] Since a paucity of cells in the fixed-film preparations contributes principally to this difficulty and a wet-film method has proved successful in the cytologic evaluation of spinal fluid where cells also may be infrequent, it was decided to apply the wet-film technique to specimens of urine from the bladder and kidney It is our purpose to present a preliminary report of these findings

MATERIALS

The urinary specimens were collected from patients at random and included voided and catheterized vesical urine, and ureteral specimens The group with confirmed diagnoses was selected for evaluation and in this there were 129 vesical specimens from 98 patients, 42 of whom had vesical carcinoma, and 45 ureteral specimens from 43 patients, 11 of whom had carcinoma (7 of the renal parenchyma and 4 of the renal pelvis) Among the vesical specimens were 29 from 19 patients who were being followed after surgical treatment of vesical tumors

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Read at annual meeting, North Central Section of American Urological Association, Cleveland, Ohio, October 3–5, 1956

[1] Sanders Cited by, Daut, R V and McDonald, J R Diagnosis of malignant lesions of the urinary tract by means of microscopic examination of centrifuged sediment Proc Staff Meet , Mayo Clin , **22** 382–386, 1947

[2] (a) Papanicolaou, G N Cytology of the urine sediment in neoplasms of the urinary tract J Urol , **57** 375–379, 1947

(b) Papanicolaou, G N and Marshall, V F Urine sediment smears as a diagnostic procedure in cancers of urinary tract Science, **101** 519–521, 1945

[3] Chute, R and Williams, D W Experiences with stained smears of cells exfoliated in the urine in the diagnosis of cancer in the genitourinary tract a preliminary report J Urol , **59** 604–618, 1948

[4] Fremont Smith, M , Graham, R M and Meigs, J V Early diagnosis of cancer by study of exfoliated cells J A M A , **138** 469–474, 1948

[5] McDonald, J R Exfoliative cytology in genitourinary and pulmonary diseases Am J Clin Path , **24** 684–695, 1954

[6] Presti, J C and Weyrauch, H M Papanicolaou examination of the urine in the diagnosis of urinary cancer I As a test in mass screening J Urol , **73** 430–434 1955

METHODS

The sediment was obtained by centrifugation of unfixed urine at 2000 rpm for 10 minutes One or two wet-film preparations were made, depending upon the amount of sediment, and, in addition, two smears were prepared on albumin-coated slides, fixed in alcohol-acetic acid fixative (95 per cent alcohol containing 3 per cent acetic acid), and subsequently stained by a modified Papanicolaou method The wet films were prepared by adding one drop of serum-toluidine blue staining fluid to one drop of urinary sediment, mixing, and applying a cover glass Some elements showed delay in staining, but the preparations were usually satisfactory for immediate study

The *serum-toluidine blue staining fluid* is prepared as follows

1 *Stock toluidine blue solution*

Toluidine blue	1 gm
Ethyl alcohol, 95 per cent	20 ml
Distilled water	80 ml

The stain and alcohol are mortared together, as the distilled water gradually is added One milliliter of glacial acetic acid usually is added to the stock solution, but *it is optional*

2 *Serum-toluidine blue staining fluid*

Equal parts (usually 10 ml) of the stock toluidine blue solution and of horse serum* are mixed together and then centrifuged The supernate is filtered into a dropper bottle and a few thymol crystals are added The resultant solution is the staining fluid To avoid bacterial contamination, the staining fluid, when not in use, generally is stored in the refrigerator

With this stain, cells in the urinary sediment show a dark-purple chromatin, red-pink nuclear sap, and cytoplasms that are variable shades of gray, pink, and blue Polychromasia is unusually brilliant in elements in urinary sediment

RESULTS

All wet films were satisfactory, cells were readily located, and were abundant—in contrast to the paucity of cytologic elements in comparable fixed films, cytologic detail was distinct (fig 1)

Bladder For the 42 patients with vesical carcinoma, findings on initial examination were positive for tumor cells in 32 (76 per cent), doubtful in 1, and negative in 9 The 9 patients in whom the reports were falsely negative had the following vesical tumors sarcoma botryoides, one patient, embryonal carcinoma, one, papilloma (papillary carcinoma, grade 1, Ash), one, papillary transitional cell carcinomas, grade 2, Ash, five, and undifferentiated carcinoma, one Eleven of the 32 positive reports were rendered on specimens from patients having transitional cell carcinoma, grade 2, Ash Among specimens from the 56 patients with no tumor, there were two false-positive reports (one patient had pyuria,

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* Difco Bacto horse serum

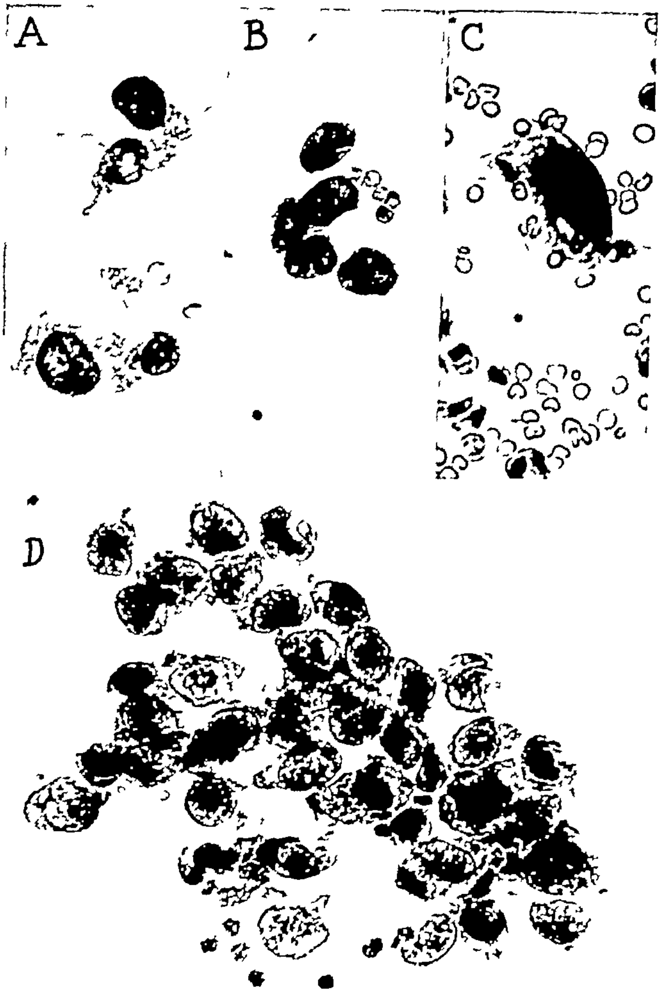

Fig 1 Carcinoma cells in vesical urinary sediments (wet films, serum toluidine blue stain) *A*, nuclei of variable size, hyperchromatism of one cell, variable nuclear cytoplasmic ratio ×450 *B*, small group of loosely arranged cells showing hyperchromasia, irregular nuclear rims and high nuclear cytoplasmic ratio ×450 *C*, tumor giant cell with large hyperchromatic nucleus and thick, irregular nuclear rim ×450 *D*, group of loosely arranged cells with sparse cytoplasm, hyperchromasia of some nuclei, irregular nuclear rims, variably sized and irregularly shaped nucleoli ×450

In *A*, *B*, and *C*, the vesical tumors were transitional cell carcinoma (grade 3 Ash), in *D*, undifferentiated carcinoma

and the other had a large obstructing benign prostatic enlargement), equivalent to an error of 5 8 per cent among all positive reports

Twenty-nine specimens were examined cytologically in conjunction with cystoscopy in the followup of 19 patients who had undergone operation for vesical cancer Three were correctly positive, 16 correctly negative, and 10 appeared to be falsely negative on the basis of clinical cystoscopic correlation

Kidney For the 11 patients with carcinoma of the kidney, findings on initial

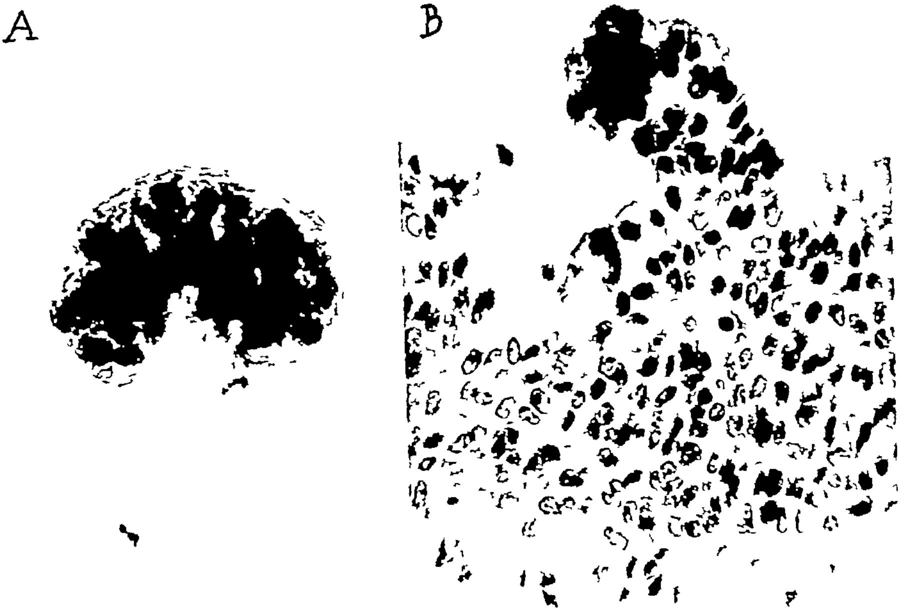

Fig 2 Papilliferous hyperplasia in calyceal epithelium, cytologically simulating papilloma *A*, circumscribed, compact mass of epithelial cells, suggesting portion of papilloma Wet film, serum toluidine blue X450 *B*, microscopic section showing papillary, nonneoplastic frond in calyceal mucosa Hematoxylin, eosin and methylene blue X450

examinations were positive for tumor cells in 5 (3 had renal cell carcinoma and 2 had transitional cell carcinoma of the renal pelvis), doubtful in 4 (2 had renal cell carcinoma and 2 had transitional cell carcinoma), and negative in 2 (each had renal cell carcinoma) There were two false-positive reports rendered on the specimens from the 32 patients who had no neoplasm Though insufficient for statistical evaluation, this would represent 29 per cent error among all positive reports In both instances where the reports were falsely positive, the patients had renal cysts with pelvic deformity In one, renal pelvic epithelial cells containing abundant granules were positive with the periodic-acid-Schiff stain, and were misinterpreted as cells of renal cell carcinoma In the second discrete, formed epithelial masses were regarded as being from papilloma (fig 2, *A*) The kidney, on pathologic examination, was found to have, in addition to two large cysts, an ulcerative, hemorrhagic pyelitis and papilliferous hyperplasia of the calyceal epithelium (fig 2, *B*)

COMMENT

In previous reports, the rate of positive cytologic findings in the presence of vesical cancer has ranged from approximately 60 to 100 per cent [2,3,4,7] In a recent study of 212 cases of carcinoma of the renal pelvis ureter and bladder,

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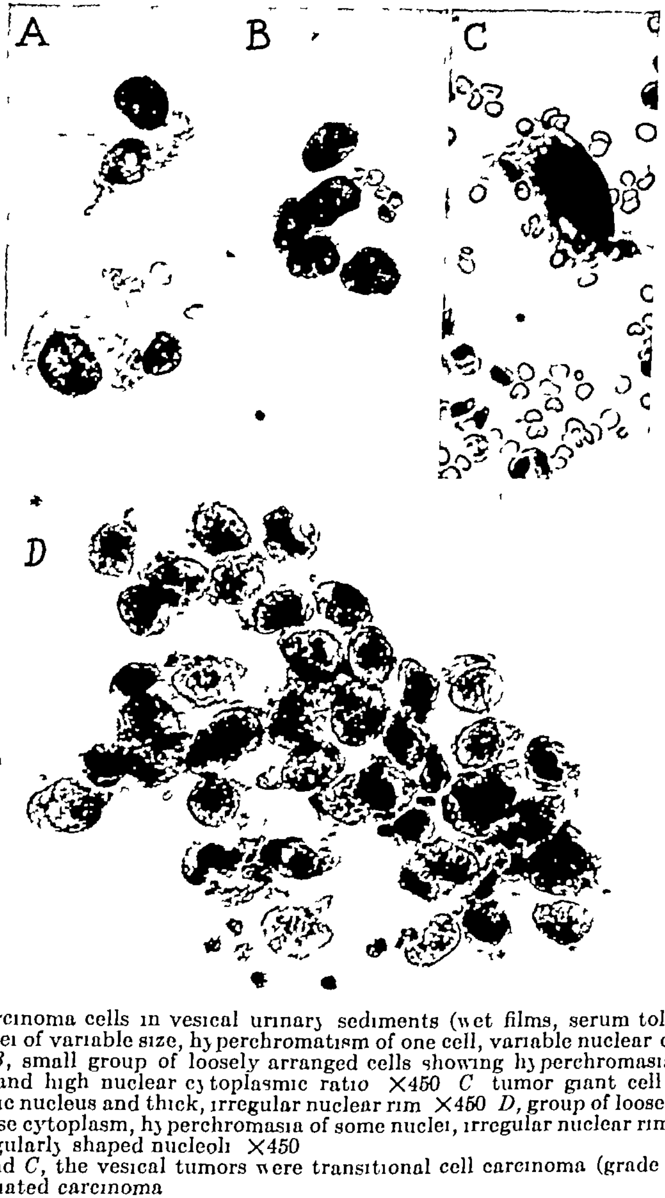
Harrison J H Botsford T W and Tucker, M R Use of the smear of the urinary sediment in the diagnosis and management of the neoplasm of the kidney and bladder Surg Gynec & Obst 92 129-139 1951



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Kidney For the 11 patients with carcinoma of the kidney, findings on initial

SUMMARY

A cytologic study of a series of urinary specimens was made utilizing a wet-film technique, in addition to fixed smears The wet method afforded a rapid means for evaluation and had the advantage of providing a maximum number of cellular elements in each preparation

The initial urinary specimens from 32 (76 per cent) of 42 patients with vesical carcinoma were positive for tumor cells Among 56 patients with no tumor, 2 false-positive cytologic reports were made on vesical urinary samples (5 8 per cent of all positive reports) Although the findings on cytologic examination were positive in 5 of 11 patients having carcinomas of the kidney (7 of renal cell type and 4 of transitional cell type), the occurrence of 2 false-positive reports in such a small series cautions against dependence on cytologic examination, at least at present, as a determining feature in decision for nephrectomy Because of the potential usefulness of the method, however, further studies seem warranted

Seybolt[8] reported the cytologic findings to be positive in 62 per cent (132) and to be suspicious in 17 per cent (36) Small tumors and even carcinoma in situ may be detected[2, 8] The rate of false-positive findings usually ranges between 2 and 8 per cent[2, 5, 8, 9]

If cytologic studies of the urine are to be made, there should be indication for their usefulness In the bladder, cytologic diagnosis occasionally has been reported as an aid in revealing the presence of a tumor which, because of its occult character or location, is not visible to the cystoscopist Though it is possible that cytologic study may provide an indication for cystoscopic examination in suspected bladder tumor, it cannot be expected to replace cystoscopy for diagnosis An important potential usefulness would be found in the followup of patients who have undergone conservative surgical treatment for vesical cancer[7] If through cytologic study some of the cystoscopic examinations for such postoperative re-evaluation could be eliminated with safety, it would reduce discomfort and expense for the patient However, as yet, there are insufficient data regarding such effectiveness to warrant a firm opinion The present short series reveals nearly one-third negative cytologic reports in patients with small tumors of the bladder interpreted as recurrences at cystoscopic examination There were no biopsies, the original tumors were transitional cell carcinoma, grade 2, Ash, and 6 of the 10 instances of negative findings were reported on specimens from two patients

The use of the cytologic method for diagnosis of renal cell carcinoma has had little support Carcinoma of the renal parenchyma may be expected to give false-negative cytologic findings since infiltration of the calyces is usually a late event Tumors of the renal pelvis should give results comparable to those in vesical carcinoma, but they are, of course, rare In the evaluation of renal, pelvic, and ureteral specimens, it is desirable to have samples from each ureter

McDonald[5] reported a false-positive rate of 31 per cent and stated he was abandoning the method for diagnosis of renal tumor A positive cytologic report may be of some assistance in supporting a diagnosis of renal tumor, but at this time must not be regarded as an indication for nephrectomy However, the obvious usefulness of the method, if dependable, warrants further effort to eliminate the hazard of false-positive reports

Wet-film preparations are readily interpreted and provide a method for rendering rapid reports Correlation with smears stained by the Papanicolaou method has been excellent, cytologic evaluation with the wet method, because of the greater abundance of cells, is much less time consuming A permanent record of the wet film may be prepared merely by separating cover glass and slide, fixing and staining the resultant smears, and reuniting slide and cover glass or mounting them separately The serum in the stain affords a good medium for holding particles of sediment for fixation

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[8] Seybolt, J F Cytology in the detection of cancer of the genitourinary tract CA, A Bulletin of Cancer Progress, 6 131–132, 1956

[9] Silverblatt, J M Exfoliative cytology as a screening test for urinary tract malignancy Bull New York Acad Med 29 889–897, 1953

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EXPERIENCES WITH THIXOKON AN AQUEOUS, THIXOTROPIC URETHROGRAPHIC MEDIUM

JOSEPH J KAUFMAN

From the Department of Surgery, Division of Urology, University of California Medical Center and Wadsworth Veterans Administration Hospital, Los Angeles, Calif

In a previous publication[1] the author has described his experience with the use of newer contrast media for urethrography In the latter phase of this study, thixokon* was used for retrograde and voiding cystourethrograms and was found to fulfill the requirements for a safe, effective urethrographic medium The purpose of this paper is to describe additional experience with this contrast medium and to emphasize its qualities as a safe, nonirritating water soluble substance of ideal viscosity and radiographic quality for use in cystourethrography and seminal vesiculography

CHEMISTRY

Thixokon is a thickened aqueous solution of the sodium salt of 3-acetamido-2,4,6-triiodobenzoic acid, an organic iodine compound, containing 65 8 per cent iodine Thixokon is thickened with amioca, a nongelling starch consisting of nearly 100 per cent amylopectin Although it is somewhat sensitive to light and must be protected from strong daylight, ordinary artificial illumination has no appreciable effect on this solution

The amioca starch not only provides the desired increase in viscosity in the thixokon solution, it also imparts a thixotropic property This means that the medium can be injected into the urethra with comparative ease, but upon coming to rest, its viscosity increases so that it may be retained during the examination

PHARMACOLOGY[2]

Injection of thixokon at 4 ml per kilogram intravenously or 0 86 ml per kilogram intraperitoneally in rats produces no untoward reactions Guinea pigs injected intraperitoneally with 2 ml of thixokon and observed for 3 months exhibit no signs of toxicity or peritoneal irritation A single application of 0 05 ml of thixokon in the conjunctival sac of rabbits' eyes produces only a mild degree of eye irritation which clears completely in 24 hours or less

The value of urethrography has been emphasized in previous publications and the technique for retrograde and voiding cystourethrograms has also been described [1] It is considered important to perform both retrograde and voiding cystourethrograms in the majority of patients suspected of having bladder neck,

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[1] Kaufman, J J and Russell, M Cystourethrography Clinical experiences with newer contrast media Am J Roentgenol , Rad Ther and Nucl Med , 75 884–892, 1956

* Thixokon is the registered trademark of Mallinckrodt Chemical Works, St Louis, Missouri, for its brand of thickened sodium acetrizoate solution

[2] Horn, H J Hazleton Laboratories, Falls Church, Virginia a) Private report to Mallinckrodt Chemical Works, April 18, 1955 b) Private report to Mallinckrodt Chemical Works May 10, 1955

prostatic or urethral disease No alteration of the technique has been made since our original report

RESULTS

We have completed 175 examinations with this medium and have been satisfied that no serious untoward reactions have resulted from its use In addition, the medium has been found to impart excellent radiopacity even when diluted to one part in three or one part in four with water or urine (e g cystography and voiding cystourethrography) Approximately one patient in four has complained of mild evanescent urethral irritation, but the clinical safety of thixokon is well demonstrated in figure 1 In this case 30 cc of undiluted thixokon was introduced into the urethra of a 60-year-old Negro using the Brodny clamp and syringe method Moderate force was exerted to overcome resistance offered by the stricture The first film demonstrates extensive urethrovascular invasion with transgression of the dye into numerous veins draining into the dorsal vein of the penis (fig 1) The patient had no pain or systemic complaints as a result of the urethrovascular invasion and 10 minutes after the injection, an x-ray film demonstrated renal excretion of the systemically absorbed medium (fig 2) The fact that the patient withstood sufficient urethrovascular invasion to produce excretory urograms of this quality is further evidence of the safety of the contrast medium when absorbed into the systemic circulation

Figure 3 demonstrates the excellent quality of urethrograms which can be obtained using standard urological x-ray equipment The viscosity and radiopacity of thixokon are ideal from the standpoint of adequately filling the urethra and at the same time preventing obscuration of intraurethral lesions by exces-

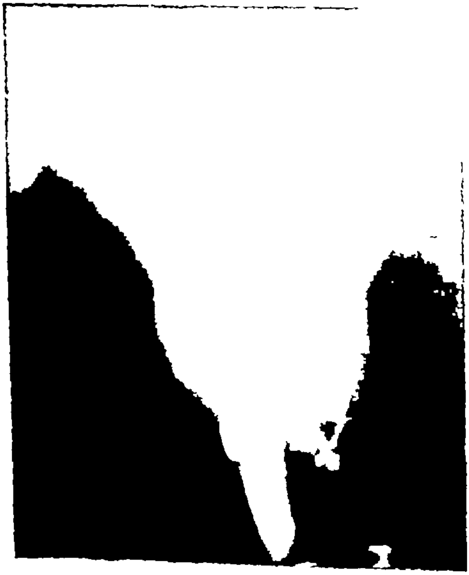

FIG 1

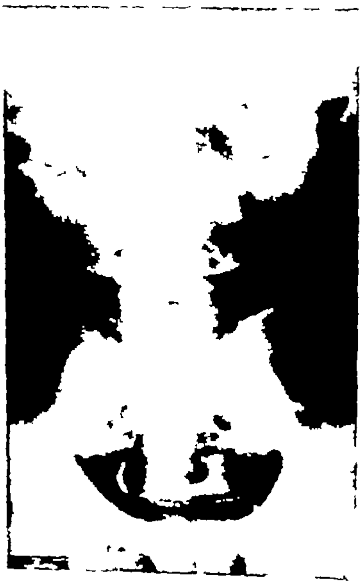

FIG 2

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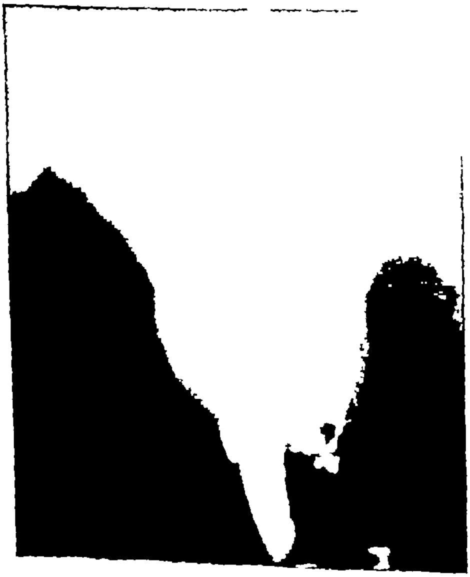

Fig 1

Fig 2

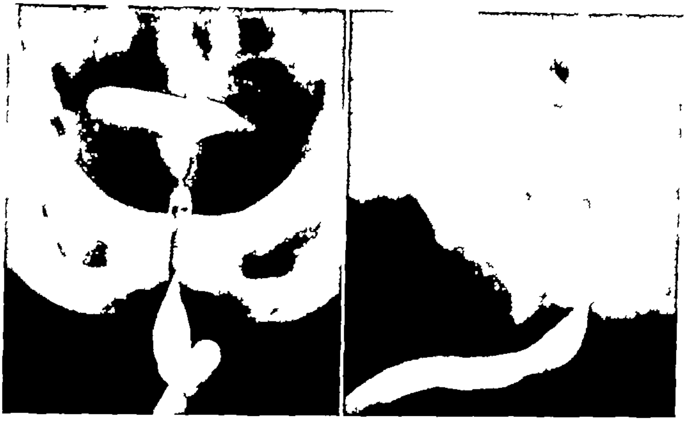

FIG 3

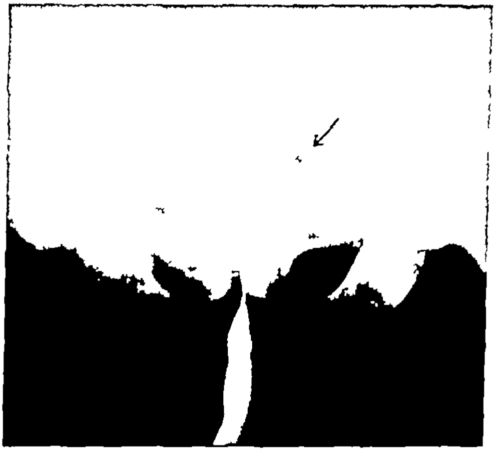

FIG 4

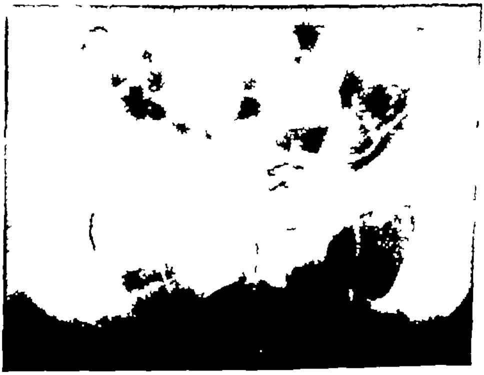

FIG 5

sive opacification The verumontanum in figure 3 is well shown as a filling defect in the prostatic urethra and the bladder neck and bladder outlines are shown by virtue of the miscibility of the contrast medium with urine and the absence of puddling

Further evidence of the desirable qualities of thixokon is shown in figure 4 In this case, a small filling defect is seen on the left side of the bladder in the cystogram produced incidental to urethrography This filling defect suggested a vesical tumor which was confirmed on cystoscopy The actual size of the papillary bladder tumor was less than 5 mm Films of this type suggest that urethrocystography can occasionally provide a screening test for the detection of urethral and bladder lesions

Thixokon, diluted with equal parts of sterile distilled water, has also been used for contrast studies of the vasa and seminal vesicles and has been found to produce good contrast, excellent filling and no undesirable side effects Figure 5 is an antegrade vasovesiculogram showing patent vasa and ejaculatory ducts, and coarsening of the seminal vesicles characteristic of chronic inflammation

CONCLUSION

Thixokon has been employed in 175 instances for producing retrograde and voiding cystourethrograms It has been found to possess excellent radiopacity in undiluted strength and also in dilutions up to one part in four parts of water It is relatively nonirritating to urethral mucosa, miscible with urine and harmless when introduced into the circulation* It is felt that thixokon deserves further trial by urologists for radiodiagnostic use in urethral, bladder neck, bladder and seminal tract conditions

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[*] The usual precautions regarding use of organic iodine salts should be taken in patients with a history of allergy

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PRACTICAL DEVICE TO REDUCE RADIATION HAZARD IN UROLOGY

MEYER EMANUEL AND FRANCIS J O'CONNOR

From the Veterans Administration Center, Togus, Maine

The advent of the atom bomb and nuclear medicine has called attention to the hazards of radiation to the general population and especially the physician who works with x-ray equipment The work of Henshaw and Hawkins, March, and Ulrich clearly indicates that leukemia is prevalent in increased incidence among radiologists as compared to their fellow physicians The data gathered by Shields Warren highly implied that ionizing radiation lowers resistance to disease and hastens the aging process in physicians who use x-rays in their daily work Radiation effects, however, are by no means only the lot of the radiologist Of 35 doctors treated at the Mayo Clinic during a 20-year period for x-ray injuries, only 8 of the entire group had been trained in x-ray procedures Apart from avoiding the local skin changes induced by excessive radiation in the form of erythema, epilation, atrophy, and occasionally late carcinoma formation, which today result only from carelessness and ignorance of the inherent dangers, the practical problem in the modern use of x-ray in diagnosis is that of minimizing x-ray exposure to the hematopoietic system and germinal cells

Among such individuals are the urologist and his assistant, who must work close to the patient when doing retrograde pyelography, cystography, urethrography, vesiculography and other procedures requiring use of x-rays Undoubtedly retrograde pyelography represents the bulk of the work that subjects a busy urologist to radiation at the cystoscopy table

The National Committee on Radiation Protection states that the maximum permissible dose (M P D) for persons between 18 and 45 years of age shall be 0 3 r (300 milliroentgens) measured in air, per week (48 hr period), and double this value for persons 45 years of age or older By means of pocket chambers, pocket dosimeters, and film badges used as monitoring devices it is possible to determine the number of milliroentgens of ionizing radiation an individual receives to various parts of the body in carrying out his work

Archer notes that the basic tolerance dose at one time was 600 mr per week instead of the present 300 mr , and that in Sweden it has been reduced to 100 mr Taylor states that even the slightest dose of radiation has some effects on the living human body and that the figure of the present 300 mr "was determined from a limited amount of clinical and biological data to which was applied a series of well-educated guesses " Considering these statements, it would appear that there is some doubt that one can rely fully on the level of 300 mr weekly, and every attempt should be made to reduce radiation to as near zero as possible Any amount of radiation, however small, is undesirable

With the objective of further reducing radiation hazard in retrograde pyelography and other urologic procedures including use of the Brodny syringe device,

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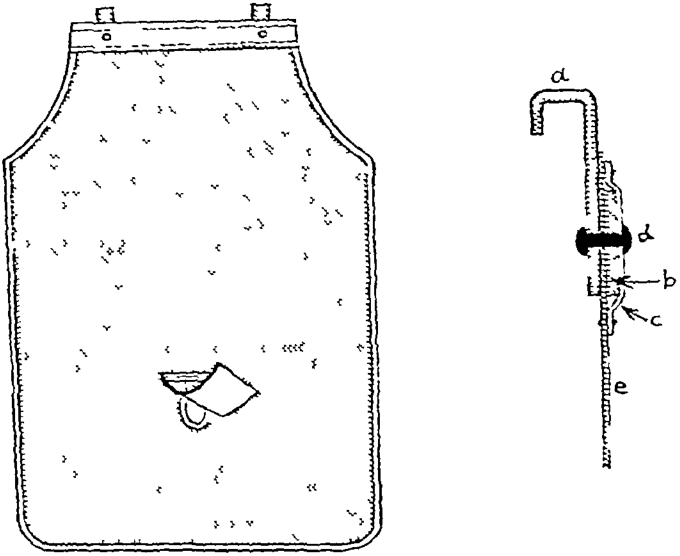

FIG 1 Apron aperture and its trapdoor flap and hooks by which apron is suspended from tube-supporting crossbar Other methods of attachment to tube arm are possible Cross-section illustrates method of attaching hooks to apron *a* Hook, *b* metal bar *c* cloth webbing, *d* rivet or nut and bolt, *e* apron

we sought a practical means of protecting not only the greater portion of the body, but the hands as well The latter are usually closest to the patient and the cystoscopic table and may be subject to both primary and stray radiation

It was obvious to us that working from behind a movable screen was clumsy if not actually impossible The usual lead-rubber apron worn by the roentgenologist at fluoroscopy should be used by the urological worker when he has to be close to the patient during an x-ray exposure Such an apron offers no protection however to the hands since they would be occupied with syringes catheters adapters or needles close to the patient and table The dexterity and sensibility of the fingers being essential in doing the pyelography naturally eliminate the use of lead-rubber gloves as used in fluoroscopy

Our solution however took the form of just such an apron but modified as follows The shoulder extensions for the straps were cut away To the remaining horizontal margin was fixed a metal bar inside a piece of tape webbing To this bar in turn was fixed a pair of hooks large enough to catch the crossbar supporting the x ray tube Thus suspended from the crossbar the apron covers the patient s thighs buttocks and genitals At the level of the genitals the apron had a hole about one and one half inches in diameter cut its margin being reinforced with leather tape material Above the hole was sewn a small flap of lead-rubber material to overlap it like a hinged trapdoor Through this hole ureteral catheters or other devices such as the Brodny urethrography syringe holder could be brought out to work upon When necessary the cystoscopic sheath could be brought out through the hole along with the catheters though in most cases we are accustomed to removing the sheath before doing pyelography Thus the hands as well as the greater portion of the body are still further protected from direct radiation

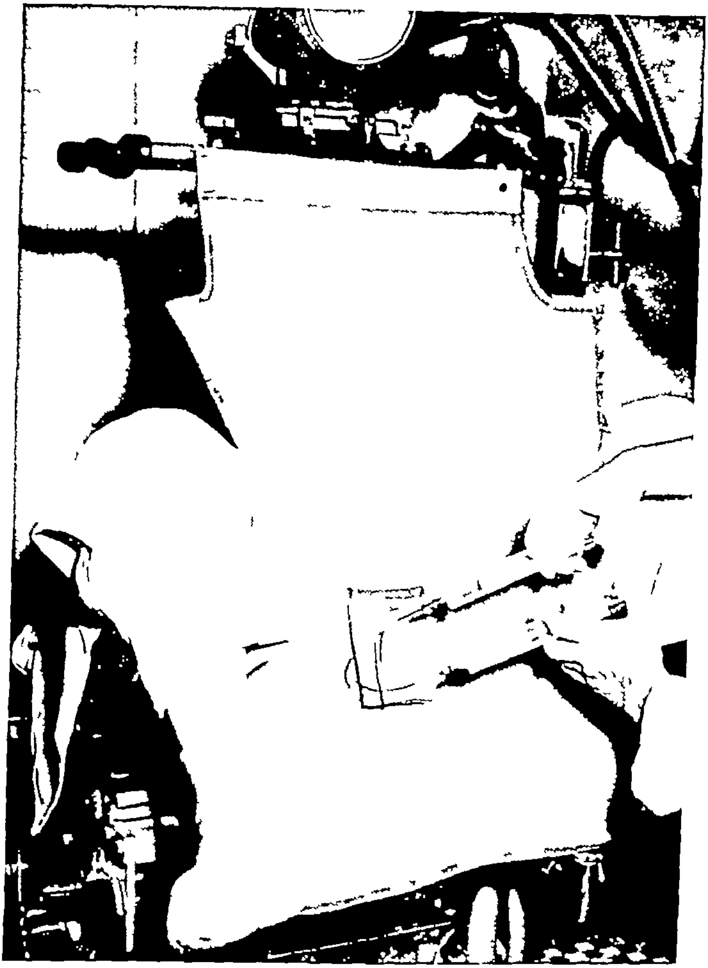

FIG 2 Apron in use in retrograde pyelography Ureter catheters emerge through hole and under trapdoor flap Measurement, made by means of pocket meter at level of hands with and without apron, indicates reduction in radiation to less than 10 per cent when lead-rubber apron is used

Although the patient is excluded from view temporarily, the gain in protection of the body and hands of the examiner far outweighs this as a disadvantage If this modified apron is hung near the cystoscopic table, it is readily accessible for use It can be applied to the tube crossbar at a moment's notice and as quickly removed This protective barrier can be prepared from readily available materials without great expense and is a definite aid to the effectiveness as a barrier in the practice of urology

Measurement made using a pocket meter at the level of the hands with and without the described protective apron indicates a *reduction in radiation to less* than 10 per cent when the lead-rubber apron is used

While interest is directed to the description of a protective device for use in urography, ready application may well be made in contrast studies on the uterus and tubes by the gynecologist, as well as generally in portable film studies by the x-ray technician

Similar devices have been used in cerebral angiography, angiocardiography, cholangiography, femoral arteriography, and lumbar aortography

We recommend this apron only in addition to the protective requirements of the National Committee on Radiation Protection in Handbook 60 and in no way as a substitute These requirements are a diagnostic type protective tube housing reducing the leakage to at most 0 10 r/hr at one meter, diaphragms or cones for collimating the useful beam and providing the same degree of protection as the tube housing (a cone covering a field of 20 inches in diameter at the film is ideal), a total filter permanently in the useful beam equal to 2½ mm of aluminum (the great majority of equipment in use today has only 0 5 mm of aluminum added filter, and new equipment is not necessarily provided with adequate filtration or cones)

SUMMARY

In the light of present knowledge there appears to be a potential hazard to the urologist and his technician from repeated exposure to radiation over a period of years A lead-rubber apron (0 5 mm Pb equivalent) modified for use at the cystoscopy table by attachment to the x-ray tube arm, is described as a means of minimizing the radiation hazard, in addition to the required diagnostic protective tube housing, use of cones or diaphragms, and 2½ mm of aluminum total filtration

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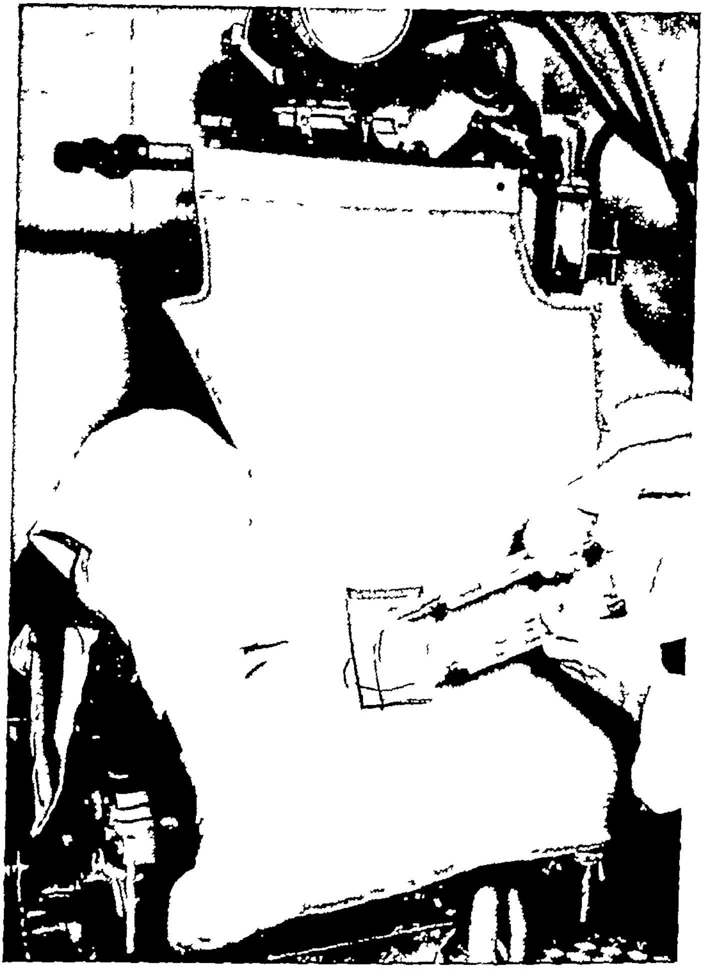

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NEPHROBLASTOMA (WILMS' TUMOR) CASE REPORT

H ANNAMUNTHODO AND R F HUTCHINGS

From the Departments of Surgery and Obstetrics, University College Hospital of the West Indies, Jamaica, B W I

Nephroblastoma was first described by Gairdner in 1828 In the late nineteenth century several cases were reported in the European literature In 1899 Wilms described in detail the pathology and discussed the histogenesis of the tumor The first successful nephrectomy for nephroblastoma was performed by Jessop in 1877

Our case is reported because of its early diagnosis, and because we believe it to be the youngest successfully treated case It illustrates the problems of investigation and treatment of nephroblastoma in the newly born It is also considered appropriate to review the clinical aspects of the disease from the now extensive literature

CASE REPORT

Following a normal pregnancy and labor, M C , a Negro male infant weighing 5 pounds, 14 ounces was delivered spontaneously at the University College Hospital of the West Indies on June 29, 1954 At the age of 6 days, on routine clinical examination, a firm, elongated, nontender mass was palpated in the left hypochondrium It extended approximately 2 cm below the costal margin and moved with respiration

Urine examination and x-ray of chest were normal In a plain x-ray of the abdomen the renal outlines were obscured by intestinal gas shadows Excretory pyelogram was performed using 15 ml of 35 per cent diodone injected into the sagittal sinus This showed the left kidney to be enlarged and the calyces slightly dilated and splayed out (fig 1, *A*) Excretion of the right kidney was obscured by intestinal gas shadows Pyelography was repeated 24 hours later, using the same technique, and a normal right kidney was demonstrated (fig 1, *B*)

On July 9, 1954, at the age of 10 days when his weight was 6 pounds, 7 ounces, the left kidney was explored Half a drachm (1 75 ml) of paraldehyde in one ounce (28 ml) of water was given rectally one hour before operation Atropine, gr 1/150, was given half an hour later Polythene tubing was introduced into the internal saphenous vein at the ankle and saline infusion commenced The infant was placed in the left kidney position and the operative site was infiltrated with 0 5 per cent novocain with 0 25 ml B P adrenaline to 100 ml Altogether only 10 ml of this anesthetic solution was used The kidney was exposed through a left oblique muscle-cutting incision extending from the tip of the twelfth rib to 1 cm in front of the anterior-superior iliac spine The kidney was mobilized extraperitoneally and delivered The renal pedicle was ligated and divided en masse During the ligation of the pedicle the infant became shocked, so further manipulation was discontinued for about three minutes Blood transfusion was started and the wound covered with a warm saline pack The ureter

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SECTION MEETINGS

Mid-Atlantic—Hotel Jefferson, Richmond, Va, October 1–4, 1958
Northeastern—White Face Inn, White Face, N Y September 12–15, 1957
North Central—Grand Hotel, Mackinac Island, Mich August 28–30, 1957
Southeastern—Hollywood Beach Hotel, Fla, January 12–16 1958
South Central—Oklahoma City, Okla, October 21–24, 1957

The Deutsche Gesellschaft für Urologie will meet in Vienna during September 1957 Details may be obtained from Prof Dr C E Alken, Univ Klinik, Homburg, Saar

Note by editor A complete list of the executive committees of the various sections, and a complete list of the officers and members of the executive committees of the various branch societies will be printed *in the December 1957* issue

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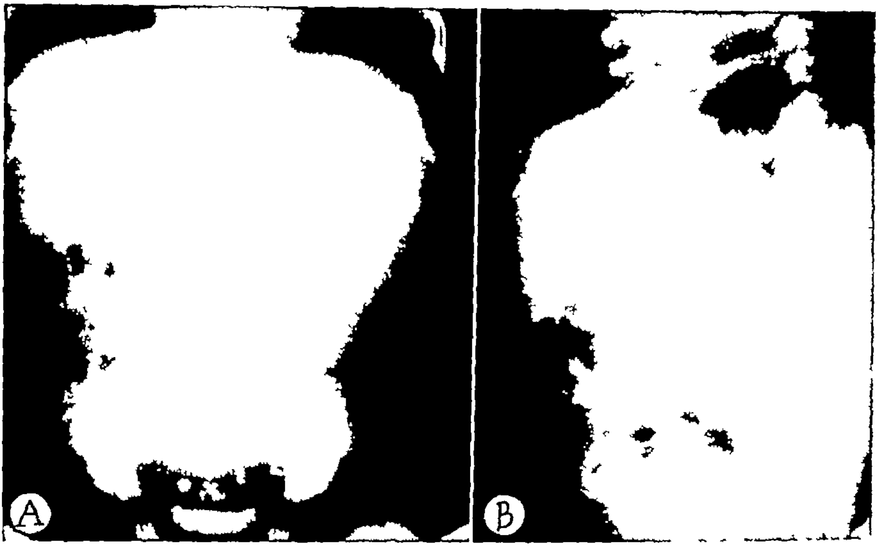


FIG 1 *A*, pyelogram shows dilated and splayed out calyces of left kidney *B*, pyelogram shows normal right kidney

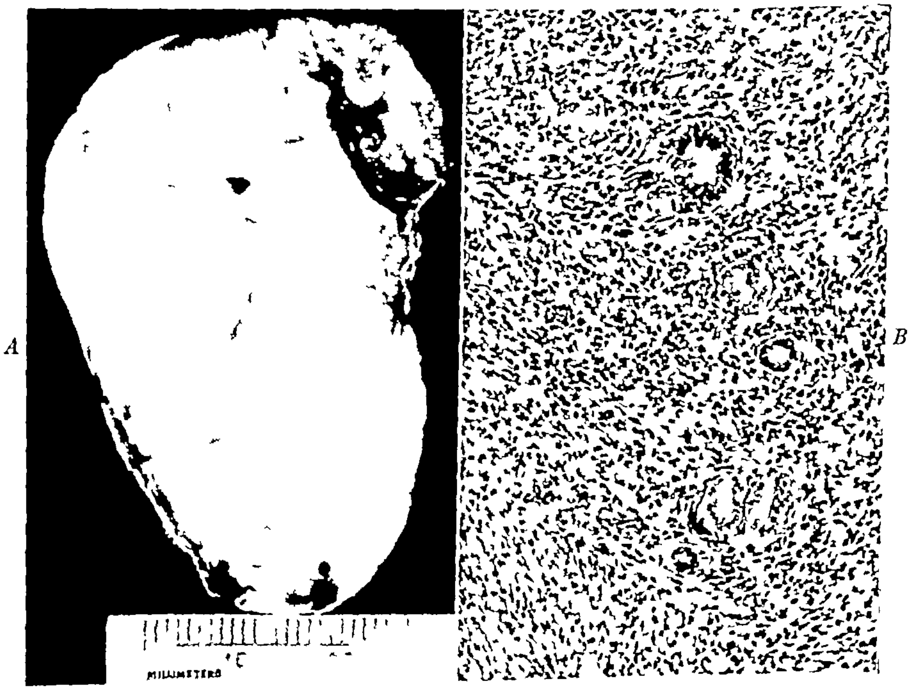


FIG 2 *A*, cross section of tumor *B*, photomicrograph (× 170)

was ligated and divided about 2 cm from the pelvioureteric junction The renal space was drained and the incision closed in layers

After 100 ml blood had been given the transfusion was discontinued During the first 8 hours the infant was given 2-ounce feeds of glucose saline and later milk, but vomited after each feed Breast feeding was then recommenced satisfactorily

Crystalline penicillin 200,000 units was given intramuscularly twice daily for 3 days

The urine output was normal after 24 hours Frequent yellow stools were passed after 24 hours and well formed stools after 48 hours

The drainage tube was removed in 48 hours, and the skin sutures on the seventh day The infant was discharged from hospital on the twelfth day after operation when his weight was 7 pounds, 9 ounces (average daily gain 1½ ounces) Two years, 7 months later his weight was 32 pounds He was fit and well and showed no evidence of recurrence

Pathology report The tumor appeared to have a definite capsule, was found to have incorporated the lower pole of the kidney and measured approximately 55 by 30 by 25 mm On cross-section (fig 2, *A*) the tumor was greyish-white with, along the edges, small areas of hemorrhage The renal pelvis and ureter were not invaded

The miscoscopic picture was typically that of Wilms' tumor (fig 2, *B*) The sarcomatous elements, as is often the case, dominated the picture

DISCUSSION

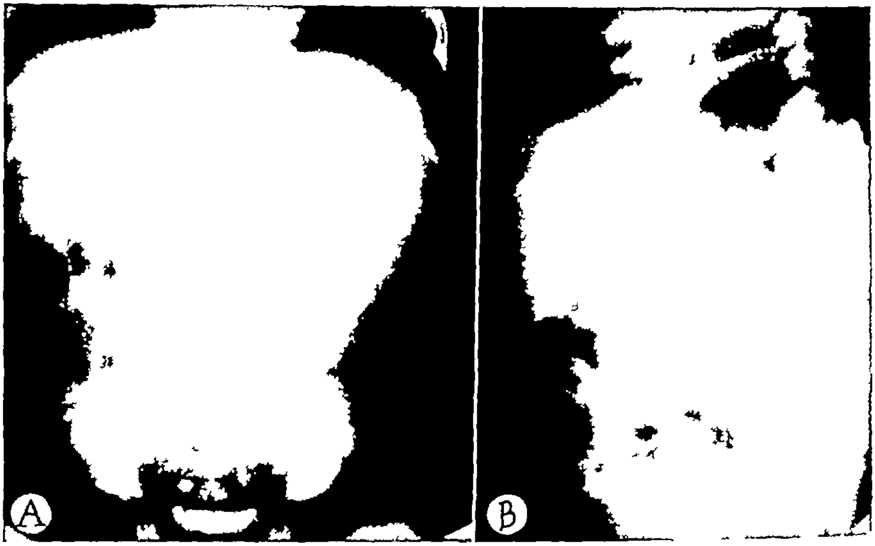
In children, with the exception of the eye, the kidney is the organ most frequently affected by malignant tumor Renal tumor accounts for 20 per cent of all cancers in children while it constitutes only 0 5 per cent in adults At the Mayo Clinic 13 nephroblastomas occurred among 271 cases of renal neoplasms, that is, 4 8 per cent (Weisel et al 1943) and in the British Isles 189 among 2,314, that is, 8 2 per cent (Riches et al 1951) The incidence among admissions to the Royal Hospital for Sick Children at Glasgow (McCurdy 1934), the Roswell Park Memorial Hospital (Sauer 1948) and the James Whitcombe Riley Hospital for Children (Garrett and Mertz 1953) was one in 3,000

Nephroblastoma is essentially a disease of infancy and childhood, the average age incidence being three to four years Table 1 shows the age incidence in the larger series of cases reported

Walker (1897) stated that 2 17 per cent of these tumors were found in the fetus and 6 7 per cent were present at birth Dean and Pack (1932) mentioned tumors in 7-month fetuses and in full-term babies, many of whom were still born Porter and Carter (1920) and Silver (1947) have reported large tumors causing dystocia Gross and Neuhauser (1950) have performed nephrectomy on a 3-weeks old infant

In our case, the tumor was palpable at the age of 6 days and can be assumed to have been present at birth

The etiology of the tumor is unknown The presence of nephroblastoma in



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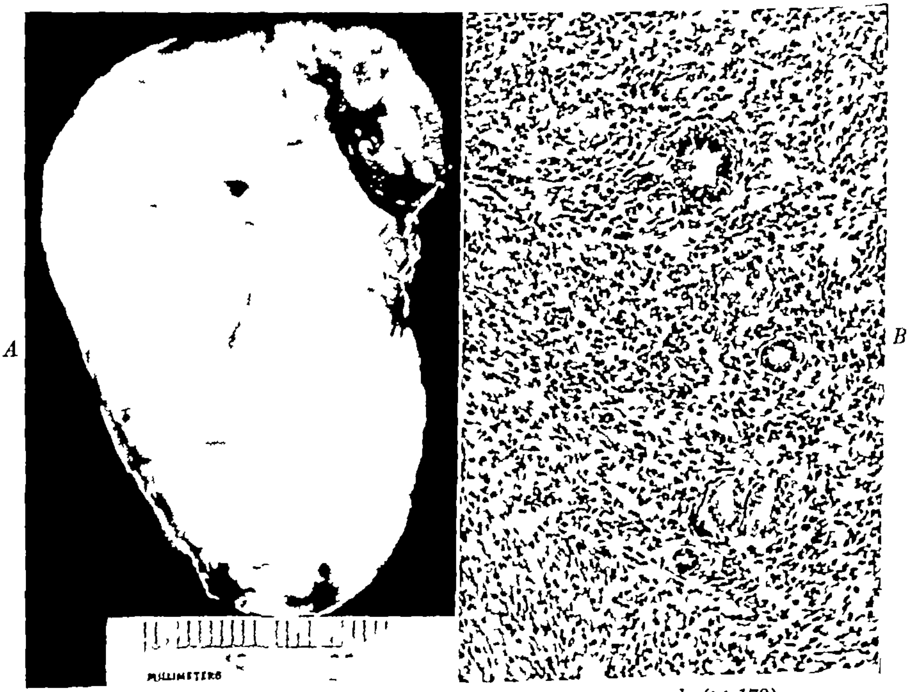

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In our case, the tumor was palpable at the age of 6 days and can be assumed to have been present at birth

The etiology of the tumor is unknown The presence of nephroblastoma in several members of the same family (Walker 1897, Deuticke 1931, Bobbio 1935, Maslow 1940) does suggest a hereditary factor in some cases

Occasionally there are associated congenital abnormalities Gaulin (1951) reported simultaneous tumors in identical twins on the right and left sides respectively This does support the theory that the nephroblastoma is a malformation rather than a true neoplasm

Kretschmer and Hibbs (1931) and Maslow (1940) obtained a history of trauma and infection in some cases Moore (1942) suggested that trauma may be a stimulus to cell activity but Hariah (1933) thought that trauma was often responsible for the discovery rather than the development of the tumor

In our case there was no history of other members of the family being affected

TABLE 1

	No of Cases	Average Age	Youngest	Oldest
Loughnane, 1914	35		3 mos	12 yrs
Mixter, 1922	17	3 yrs 6 mos		
Magoun & MacCarty, 1923	7		1 yr 8 mos	7 yrs
Hyman, 1925	10		9 mos	9 yrs
Hunt & Hager, 1929	13	4 yrs	1 yr 8 mos	7 yrs
Lieberthal, 1931	7	2 yrs 7 mos	6 mos	7 yrs
Kretschmer & Hibbs, 1931	17		3 mos	6 yrs 6 mos
Dean & Pack, 1932	16	3 yrs		37 yrs
McCurdy, 1934	27	Under 3 yrs		
Bradley & Pincoffs, 1938	5	2 yrs 5 mos	2 mos	6 yrs
Kerr, 1939	14	3 yrs 3 mos		6 yrs
Adams & Hunt, 1939	5	3 yrs	1 yr 9 mos	6 yrs
Ladd & White, 1941	60	Under 3 yrs	2 mos	9 yrs
Weisel et al , 1943	44	35 under 7 yrs	7 mos	59 yrs
Melicow, 1944	9	All under 4½ yrs	1 week*	4½ yrs
Nesbit & Adams, 1946	16	15 under 6 yrs	6 mos	
Silver, 1947	18	15 under 6 yrs	3 days†	27 yrs
Daw, 1948	7	All under 4 yrs		
Sauer, 1948	16	3 yrs	1 day‡	11 yrs
Bradley & Drake, 1949	12		1 yr	8 yrs
Senger et al , 1950	6	All under 4½ yrs	5 mos	4 yrs 6 mos
Goddard, 1950	39	37 under 7 yrs	Under 6 mos	9 yrs
Gross & Neuhauser 1950	96	Majority under 4 yrs	3 wks	
Riches et al , 1951	189	50% 2–4 yrs		
Brown, 1951	13		8 mos	8 yrs
Rusche, 1951	40	60% under 3 yrs	3 mos	10 yrs
Garrett & Mertz, 1953	24	16 under 3 yrs	6 mos	11 yrs

* Complete report not given

† Operation performed at age of 1 month

‡ Metastases present at birth

nor was there any history of trauma or infection of the infant after birth or of the mother during pregnancy

The presenting symptom in over 80 per cent of cases is a mass which may increase rapidly in size due to hemorrhage into it Bland-Sutton (1917) reported a tumor weighing 36 pounds The danger of repeated palpation of the tumor has been stressed by White (1951) and others Hematuria occurs late and conveys a bad prognosis

In this patient the tumor was small and found only on careful examination In a child of this age the tumor may easily be missed unless it is looked for There was no hematuria and no evidence of pain

In every case an excretory pyelogram should be done There is no characteristic picture, it varies from absence of excretion to varying degrees of distortion of the calyceal or pelvic pattern The main value, however, is in determining the presence and normality of the contralateral kidney and in differentiating from other kidney lesions, for example, hydronephrosis, polycystic kidney, etc , which produce characteristic pictures

In infants intravenous pyelography may be impossible Beer and Theodore (1934), Nesbit and Douglas (1939) and Brown (1951) have obtained satisfactory visualization by subcutaneous injection of diodrast The rate of absorption of the diodrast may be increased by use of hyalase Others prefer intramuscular injection (Adams and Hunt 1939)

In our patient, good visualization was obtained after injection of 15 ml of 35 per cent diodone into the sagittal sinus Because of intestinal gas shadows obscuring the contralateral renal pelvis, it was necessary to repeat the examination We have since obtained satisfactory pyelograms on infants 2 days and 4 days old by this method Intrasagittal injection is simple and harmless, and better pictures are obtained by this method than by subcutaneous or intramuscular injection Obviously, its use is restricted to the young infant

Ascending pyelography is unnecessary as a routine procedure In the male infant, it is traumatic, requires a general anesthetic and may cause delay in treatment

X-ray of the chest should be taken in all cases as pulmonary metastases often appear early Perineal or intraperitoneal air sufflation and aspiration biopsy are of doubtful value and may be dangerous

Nephrectomy as the primary method of treatment is accepted Many authors favor a transperitoneal approach as it gives a better exposure and permits early ligation of the pedicle and ureter and better exploration for metastases, but Culp and Hartman (1948) advise it only for the very large tumors For the small tumor, adequate exposure is obtained by a posterolumbar extraperitoneal approach

In most cases inhalation anesthesia has been used Deming (1923) and Walters and Priestley (1934) have used local anesthesia A large amount of novocain injected into the tissues may be toxic to the infant In our case, adequate anesthesia was obtained by the injection of only 10 ml of 0 5 per cent novocain The infant became shocked when traction was applied to the renal pedicle Deming (1923) found the same This would probably not have occurred had the pedicle been infiltrated with the anesthetic solution The use of local anesthesia is obviously restricted to infants with small tumors and is probably satisfactory only when the kidney is exposed extraperitoneally

While cures have been reported from treatment by irradiation only (Dean 1945, Whitehouse and Lampe 1953), this method of treatment is generally considered unreliable Irradiation is usually employed in conjunction with nephrectomy but there is no agreement as to the relative values of preoperative and postoperative irradiation Ladd and White (1941) and Gross and Neuhauser (1950) doubt whether the prognosis is improved by preoperative irradiation and suggest the possibility of dissemination during therapy The value of postopera-

TABLE 2

	No of Cases	Probable Cures	Length of Survival	Time of Recurrences
Loughnane, 1914	35	4	Over 3 yrs	
Mixter, 1922	17	1	3 yrs 6 mos	Within 18 mos
Magoun & MacCarty, 1923	7	1	1 yr 6 mos	Within 12 mos
Hyman, 1925	10	0		Within 12 mos
Hunt & Hager, 1929	13	1	7 yrs	Within 13 mos
White, 1931	9	2	Over 4 yrs	Within 12 mos
Kretschmer & Hibbs, 1931	17	?1		
Dean & Pack, 1932	16	0		Most within 9 mos
McCurdy, 1934	27	0		Most within 12 mos
Priestley & Broders, 1935	65	4	2 over 3½	
Campbell, 1937	55	5	Over 1 yr	Most within 4 mos
Bradley & Pincoffs, 1938	5	0		
Kerr, 1939	14	1	Over 4 yrs	
Adams & Hunt, 1939	5	?2		Within 6 mos
Ladd & White, 1941	60	14	Over 18 mos	Most within 9 mos
Weisel et al , 1943	44	7	5 over 5 yrs	Most within 12 mos
Melicow, 1944	9	1	4 yrs 6 mos	
Nesbit & Adams, 1946	16	8*	Over 3 yrs 6 mos	Within 6 mos
Dean, 1945	20	5†	Over 5 yrs	
Silver, 1947	18	10	Over 2¼yrs	
Daw, 1948	7	3	Over 2 yrs	Within 9 mos
Sauer, 1948	16	1	Over 9 yrs	Most within 6 mos
Culp & Hartman, 1948	4	1	1 yr 6 mos	Within 4 mos
Bradley & Drake, 1949	12	2	Over 5½ yrs	
Senger et al , 1950	6	1	Over 6 yrs	All within 2 yrs
Goddard, 1950	39	5	Over 4 yrs	All within 19 mos
Gross & Neuhauser, 1950	96	32	Over 18 mos	Within 9 mos
Riches et al , 1951	189	21	Over 3 yrs	
Brown, 1951	13	3	Over 1 yr	
Rusche, 1951	40	6	Over 5 yrs	Most within 12 mos
White, 1951	28	4	Over 5 yrs	
Garrett & Mertz, 1953	24	8	Over 2 yrs	

* One case treated by irradiation only

† Treated by irradiation only

tive irradiation is difficult to evaluate The importance of screening the vital organs and keeping a careful check on the blood cells during irradiation has been stressed Epiphyseal arrest (Silver 1947, Garrett and Mertz 1953) and agranulocytosis (Barr and Schulte 1950) have been reported

With early diagnosis, controlled transfusion and improvement in anesthetic and operative techniques, mortality from operation has fallen and cure rate has increased No patient with metastases has been cured by any form of treatment Gross hematuria, marked loss of weight, gross anemia and fixity of the growth are poor prognostic signs

Ladd and White (1941) and Weisel et al (1943) found that the degree of cellular differentiation had no bearing on the prognosis but that the degree and extent of hemorrhage and necrosis, rupture of the capsule and invasion of the renal vein had

The prognosis is not affected by the duration of symptoms (Kerr 1939) but there appears to be some relation between age of patient and survival rate Ladd and White (1941) and Gross and Neuhauser (1950) have reported 50 per cent and 80 per cent cure rate during the first year of life This may be due to earlier diagnosis

Recurrence rate after operation is high Late recurrences even up to ten years have been reported but nearly all recurrences occur within nine months Recurrence after one year is unusual and Campbell (1937) regards 1-year survival with no evidence of recurrence as cured Ladd and White (1941) and Gross and Neuhauser (1950) accept 1½ to 2-year survival as cured The cure rate and time of recurrence in the larger series of cases are shown in table 2

It is probably too soon to say what the end result of this case will be There was no evidence of metastases at the time of operation The histological picture showed a high degree of cellular differentiation and there was no evidence of renal vein involvement

The child is now 2 years, 7 months old with no evidence of local recurrence or distant metastases and the prognosis can therefore be regarded as good

SUMMARY

A case of nephroblastoma in a 6-day old infant, treated by nephrectomy only, is reported This is probably the youngest successfully treated case

The importance of thorough routine physical examination of infants is stressed

Intrasagittal injection for pyelography is mentioned as an alternative to intravenous, subcutaneous and intramuscular injection

Local anesthesia is recommended for nephrectomy in infants with small tumors

The literature on the clinical aspect of the disease is reviewed

We are grateful to Professor D B Stewart, Department of Obstetrics, University College of the West Indies, for his interest in the preparation of this case report

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MULTIPLE DISSIMILAR TUMORS IN ONE KIDNEY

SALVATORE A PENNISI, SIMON RUSSI AND R CARL BUNTS

From the Urological Section, Surgical Service and Pathology Section, Laboratory Service, McGuire Veterans Administration Hospital, Richmond, Va

A review of the literature reveals infrequent case reports of multiple dissimilar tumors in one kidney [1-21] Only one case report of three dissimilar tumors in the same kidney was found Wildbolz reported a patient with a pelvic papilloma, papillary carcinoma and hypernephroma in a single kidney [1] Another report of three dissimilar tumors follows

CASE REPORT

No 48-4875 A 52-year-old white man was admitted to the urology service on March 19, 1953 because of colicky right flank and right lower quadrant pain of 4 weeks' duration Intermittent gross hematuria had been noted for 5 weeks prior to this admission The hematuria became progressively severe until 2 days prior to hospitalization at which time it ceased

Examination disclosed a balding, edentulous white man in no acute distress Abdominal examination showed voluntary right sided rigidity with a right pararectus, periumbilical area of moderate tenderness, measuring about 5 by 10 cm No palpable abdominal organs were found An asymptomatic, right, incomplete, indirect inguinal hernia was also found Rectal examination showed a grade 2 symmetrical, firm prostate Questionable enlargement of the right seminal vesicle was noted

Laboratory examination Hemoglobin 13 1 gm per cent White blood cells 10,100 with 79 per cent neutrophils and 21 per cent lymphocytes Blood urea nitrogen 13 gm per cent Serology Negative cardiolipin Urinalysis pH 5 5, specific gravity 1 025, slight trace of albumin, no sugar, 15–16 red blood cells and 1–3 white blood cells per low power field

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No. 48-4875. A 52-year-old white man was admitted to the urology service on March 19, 1953 because of colicky right flank and right lower quadrant pain of 4 weeks' duration. Intermittent gross hematuria had been noted for 5 weeks prior to this admission. The hematuria became progressively severe until 2 days prior to hospitalization at which time it ceased.

Examination disclosed a balding, edentulous white man in no acute distress. Abdominal examination showed voluntary right sided rigidity with a right pararectus periumbilical area of moderate tenderness measuring about 5 by 10 cm. No palpable abdominal organs were found. An asymptomatic right incomplete indirect inguinal hernia was also found. Rectal examination showed a grade 2 symmetrical firm prostate. Questionable enlargement of the right seminal vesicle was noted.

Laboratory examination. Hemoglobin 13.1 gm. per cent. White blood cells 10,100 with 79 per cent neutrophils and 21 per cent lymphocytes. Blood urea nitrogen 13 gm. per cent. Serology: Negative cardiolipin. Urinalysis: pH 5.5, specific gravity 1.025, slight trace of albumin, no sugar, 15–16 red blood cells and 1–3 white blood cells per low power field.

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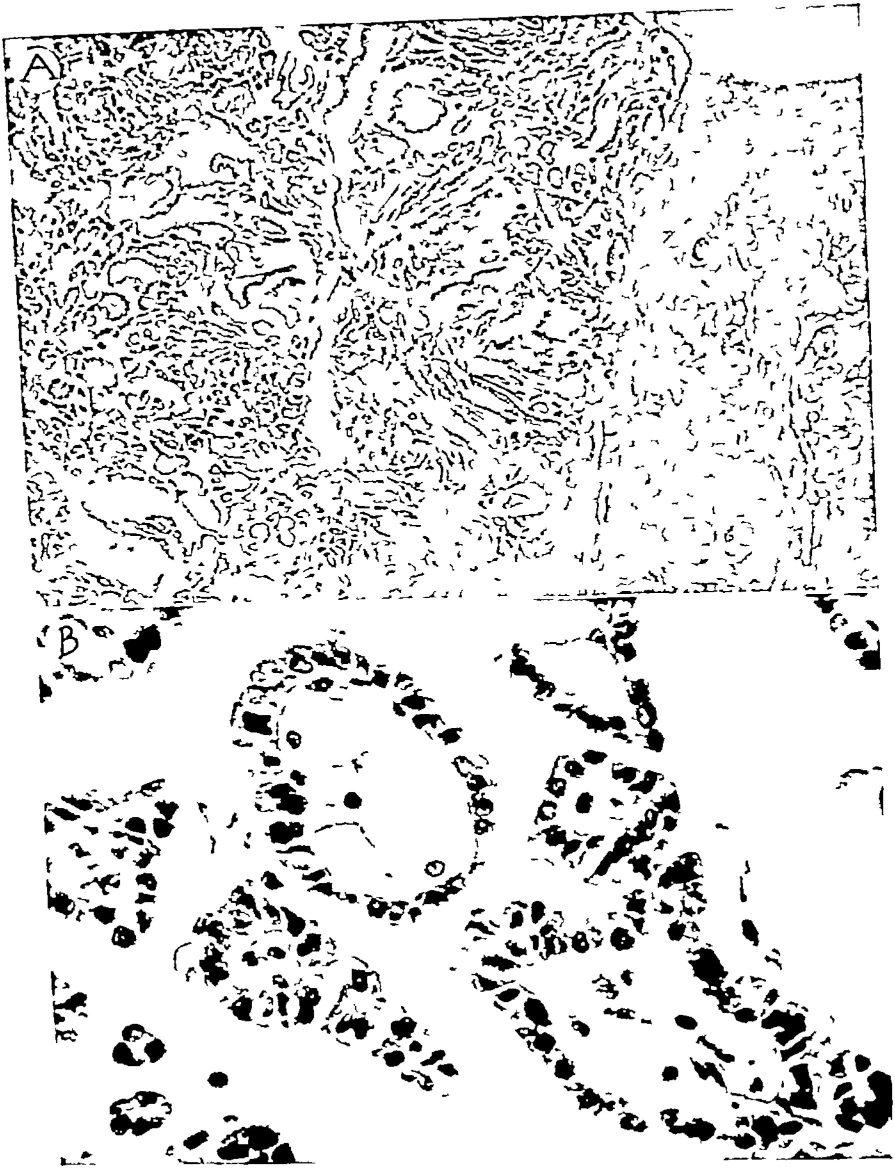

Fig 3 A, low power photomicrograph B, high power photomicrograph of cystadenoma showing papillary fronds covered by somewhat atypical cuboidal epithelium containing large pale lipophages in stroma

A translumbar aortography and paracoccygeal oxygen insufflation on March 23 did not reveal any gross abnormality of the kidneys Exploration of the right kidney on March 25 revealed a small, solid, 1 5 cm nodule on the lower convex surface and a hard nodular pelvis A right nephrectomy was performed Postoperative course was uneventful

Cystoscopy on March 20 showed blood coming from the right ureteral orifice Retrograde pyelography visualized an irregularity of configuration of the right pelvis and calyces (fig 1) The left kidney appeared normal There was no indigo carmine dye excretion from the right and normal excretion from the left ureter

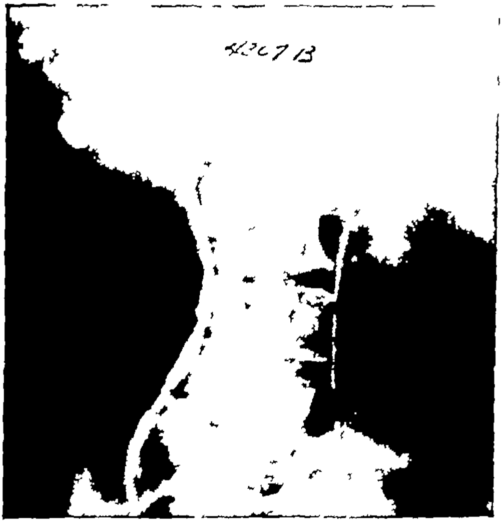

Fig 1 Right retrograde pyelogram demonstrates incomplete filling

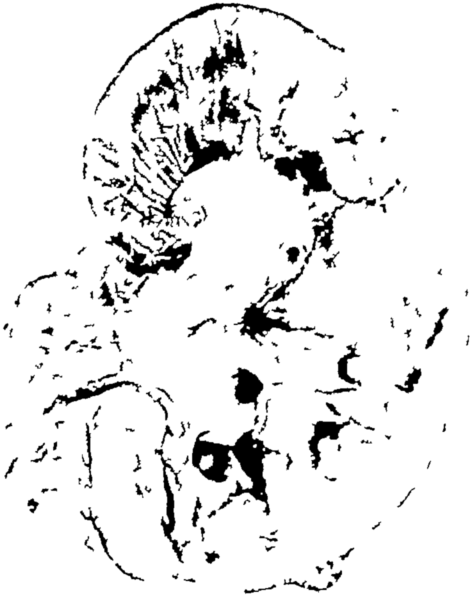

Fig 2 Cross section of kidney shows adenoma at lower pole and papillary tumor of pelvis

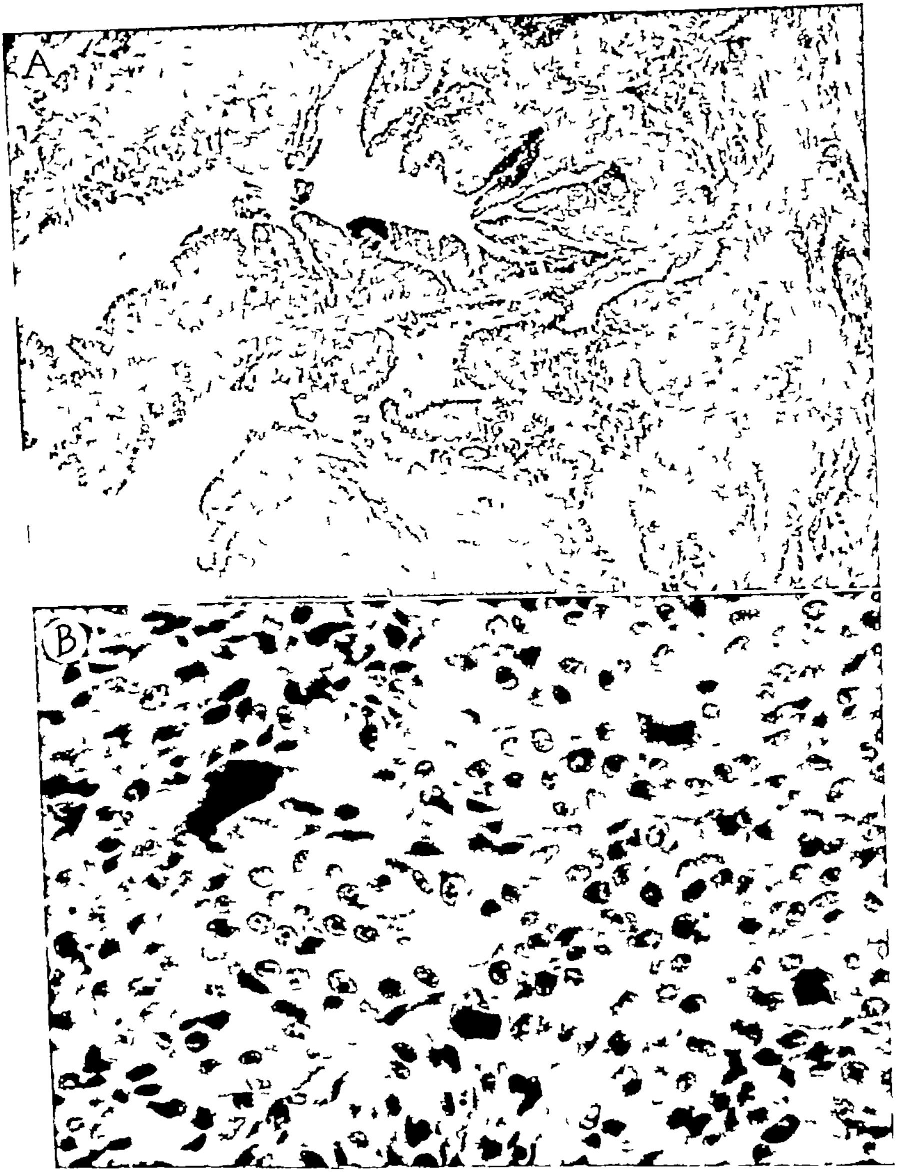

FIG 5 A low power photomicrograph of pelvic tumor shows papillary projections composed of stratified transitional epithelium supported by slender connective tissue stalks B high power photomicrograph of pelvic tumor shows cellular pleomorphism with few grotesque nuclear masses

presented the usual configuration of cortical and medullary tissue The cortex measured 7 mm in thickness A slight amount of peripelvic fat was present A sessile, papillary lesion was present in the lower part of the pelvis at its junction with the ureter The lesion was roughly oval-shaped, measuring 3 cm in the long

Pathology report The gross specimen consisted of the right kidney which was bean-shaped and measured 11 cm from pole to pole, 6 5 cm in width and 3 5 cm in thickness (fig 2) The capsule stripped with ease revealing a smooth, pale reddish-brown, cortical surface with a few fetal lobulations The cut surface

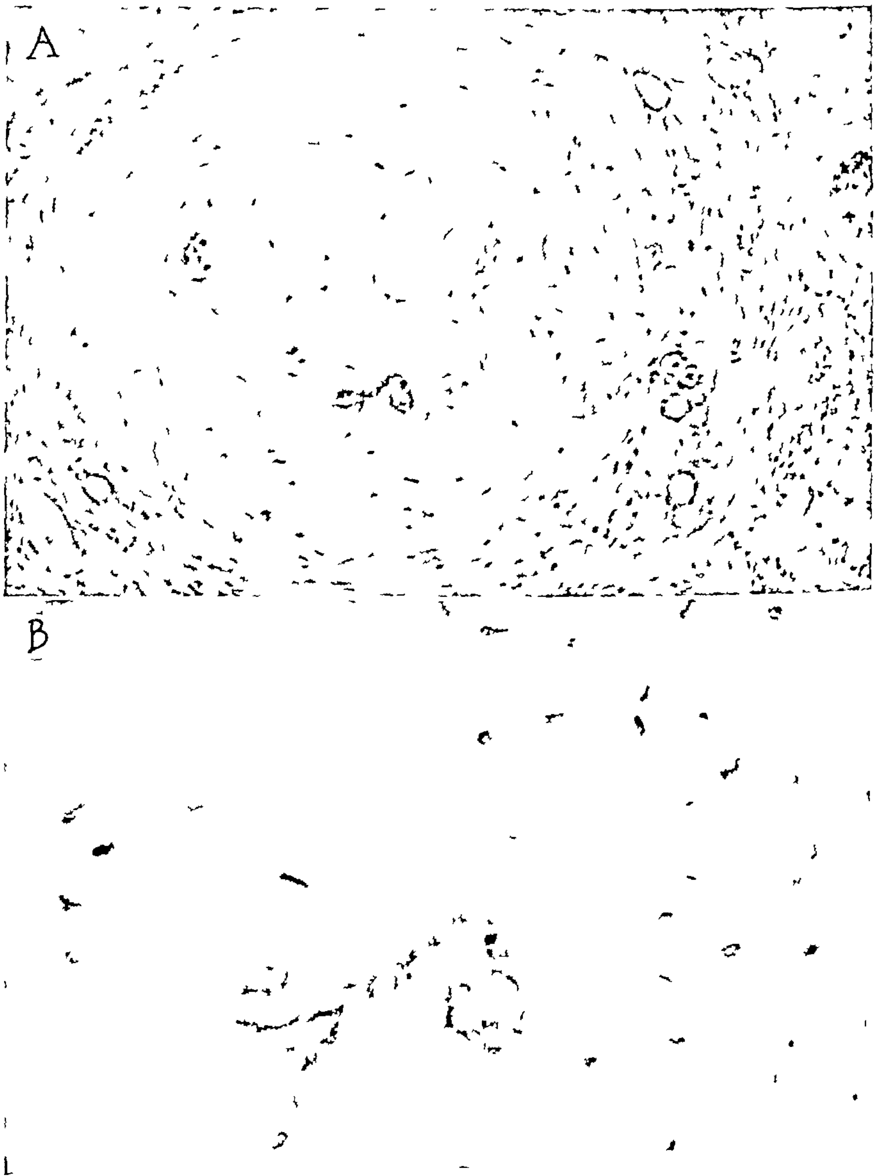

FIG 4 *A*, low power photomicrograph shows discrete, nonencapsulated, myxomatous nodule with trapped tubular structure *B*, high power photomicrograph shows myxomatous stroma surrounding epithelium lined tubular structure

A discrete, nonencapsulated nodule was seen in the cortex Its external surface was rounded and bulged into the capsule The nodule was made up of multiple cystic concamerations filled by slender papillary or club-shaped fronds (fig 3, *A*) The walls and the papillary projections were covered by a single layer of cuboidal or low columnar epithelium The cells and their nuclei showed some variation of size The nuclei varied in shape and intensity of staining and showed some distortion of polarity The stroma of the papillary processes contained in many instances large, pale polygonal cells with a pale, finely granular cytoplasm and eccentric bland nuclei (fig 3, *B*) Although the cellular morphology of the lesion and its lack of encapsulation were somewhat disturbing, the small size of the lesion made us decide in favor of the diagnosis of papillary cystadenoma In addition to this lesion, several nodules of microscopic proportions were scattered through the parenchyma of the kidney They were round or oval structures made up of a pale myxomatous stroma supporting somewhat distorted, scanty tubular elements lined by cuboidal epithelium The nodules displaced the neighboring elements of kidney parenchyma (fig 4, *A*) and were well demarcated but not encapsulated The stromal cells were stellate or spindle-shaped with anastomosing fibrillar, cytoplasmic processes in a pale homogeneous matrix The epithelial structures were curved tubules lined by somewhat distorted cuboidal cells (fig 4, *B*) These nodules were classified descriptively as myxoadenomas The pelvic lesion was made up of a luxuriant overgrowth of transitional epithelium forming numerous papillary projections supported by slender connective tissue stalks (fig 5, *A*) No downgrowth of epithelium into the pelvic wall could be demonstrated There was a fairly dense layer of lymphocytic infiltration within the lamina propria at the base of the lesion The individual epithelial cells presented an orderly pattern of transitional epithelium undergoing hyperplasia However, in a few areas, there was considerable pleomorphism and atypical mitotic activity (fig 5, *B*) which suggested the pathologic diagnosis of transitional cell carcinoma of the renal pelvis Examination of the ureteral segment revealed no significant pathologic changes In summary, a single kidney presented a 1) papillary cystadenoma, 2) multiple myxoadenomas and 3) papillary transitional cell carcinoma of the renal pelvis

COMMENT

Berry reported 4 cases of synchronous different tumors in one kidney [2] Graves and Templeton in reporting two cases remarked, 'Combined renal tumors are rare '[3] DeVries reported a case of two tumors involving one side of a horseshoe kidney [4] Balch reported a case of two different neoplasms involving one kidney [5] In their discussion of the relation between adenoma and carcinoma of the kidney, Cabot, and others incidentally mentioned that they saw several cases where a kidney grossly showed 'both a carcinoma and single or multiple adenomas '[6] These reports along with others are tabulated in table 1

SUMMARY

A case report of three dissimilar tumors in one kidney is presented along with tabulation of reports of synchronous dissimilar tumors in one kidney

TABLE 1 *Multiple dissimilar tumors in one kidney*

Author	Year	Side	Age	Sex	Tumors
Berry[2]	1919	Right	43	F	Adrenal cell carcinoma, fibrosarcoma
		Left	35	F	Adenocarcinoma, fibrosarcoma
		Right	72	M	Hypernephroma, leiomyosarcoma
			51	M	Adrenal tumor, renal cell adenoma
Graves & Templeton[3]	1921	Left	52	M	Papillary carcinoma of pelvis, hypernephroma
		Right	52	M	Papilloma of pelvis, papillary cyst adenoma of kidney
Patch & Rhea[7]	1924		68	M	Papilloma of pelvis, papillary adenocystoma of kidney
DeVries[4]	1930	Left	57	M	Papilloma of pelvis, hypernephroma
Judd & Donald[8]	1932				Adenocarcinoma, fibrosarcoma
Wildbolz[1]	1933				Papilloma of pelvis, papillary carcinoma, hypernephroma
Balch[5]	1935	Left	63	M	Papillary carcinoma, hypernephroma
Chwalla[9]	1936				Hypernephroma, sarcoma
Mintz[10]	1937	Right	48	M	Spindle cell sarcoma, squamous cell carcinoma of pelvis
		Right	53	M	Adenocarcinoma, fibrosarcoma
Dick[11]	1942	Left	51	M	Renal cell carcinoma, papilloma of pelvis
Weisel & Dockerty[12]	1942	Right	48	M	Adenocarcinoma, fibrosarcoma
		Left	68	M	Adenocarcinoma, fibrosarcoma
Riopelle[13]	1945	Left			Epitheliosarcoma, lipofibromyoma
Olsterlin[14]	1945	Right	57	M	Wilms' tumor, adenocarcinoma
Melicow[15]	1945	Right	65	M	Papillary epithelioma of pelvis, clear cell carcinoma of kidney
Cristol, and others[16]	1946				22 cases of Grawitz tumor with papillary adenoma
Macalpine[17]	1947	Left	72	F	Papillary carcinoma of pelvis, renal adenoma
Rupel & Sutton[18]	1950	Left	58	F	Papillary carcinoma of pelvis, adenocarcinoma
Bhende[19]	1952	Left	35	M	Epidermoid carcinoma, leiomyosarcoma
Kline, and others[20]	1955	Left	47	M	Transitional cell carcinoma, adenocarcinoma
Young & Deming[21]	1955	Right	44	M	Papillary adenoma and carcinoma

diameter and 2 5 cm in the short diameter It projected above the surface of the pelvis for a distance of 4 to 6 mm It had a pinkish-yellow, friable, finely granular surface The major calyces were moderately dilated The cut surface of the lesion was pink and it seemed to be confined to the inner half of the pelvic wall At the lower pole of the kidney, just beneath the capsule, a round nodule measuring 1 cm in diameter was seen The nodule had a mealy, dark brown cut surface A segment of the right ureter was also present and the entire segment was patent At the proximal end of the ureter, the surrounding connective tissue was thickened and indurated Histologic sections of the kidney were reviewed

CASE REPORT

C W (017-9-29), a 5-year-old Negro girl was admitted to the University Hospital June 10, 1955 for urologic survey because of complaints by her parents that the child "wet the bed" and dribbled urine during the day in addition to voiding apparently normal amounts of urine at regular intervals The child had never been completely dry since birth She had been followed in the pediatric outpatient clinic where complaints of urinary frequency, dribbling, enuresis and diurnal incontinence were noted Shortly before this admission an intravenous urogram showed bilateral renal function and was reported negative

General physical examination on admission showed a healthy girl The only abnormal finding was a clear, watery discharge from the urethral meatus, present even after the child voided in normal amounts No other congenital abnormalities were noted Rectal examination was negative Neurologic examination was negative After voiding 200 cc clear urine, catheterization obtained 25 cc residual urine Urine culture yielded E coli, Proteus, and hemolytic Staph aureus An intravenous pyelogram showed a normal right upper urinary tract with reduplication of the left renal collecting system The ureters were not well visualized in these films At cystoscopy on June 18, 1955, no ectopic orifice could be visualized A normally situated left ureteral orifice was catheterized and a pyelogram showed filling of a normal pelviocalyceal system representing the lower segment of the reduplicated kidney A subsequent cystoscopic examination disclosed the orifice of the ectopic ureter leading to the upper half of the left kidney It was situated just inside the external meatus of the left lateral wall of the urethra It was catheterized as well as the normally situated left orifice in the bladder A simultaneous pyeloureterogram demonstrated the reduplicated collecting system with the ectopic ureter inserting into the urethra responsible for the child's incontinence

On June 29, 1955, renal exploration was done in order to accomplish heminephro-ureterectomy Upon exposing the kidney a yellow-white, irregular nodule was seen arising from the anterior surface of the kidney 3 cm below the cortical indentation that separated the two collecting systems Wedge resection of this area was done and frozen section obtained, which was equivocal because the pathologist reported renal epithelial cells in a somewhat tumorous arrangement but could not state whether this represented a malignant change or not Since the area in question seemed to be completely excised, we decided to perform heminephrectomy and ureterectomy to the brim of the pelvis at this operation The patient withstood the procedure well and permanent sections of the kidney tumor showed it to be a renal cell adenocarcinoma There was no doubt in the minds of our Pathology Department that this represented a malignant change and not a simple adenoma (fig 1)

The slides were reviewed by Dr F K Mostofi of the Armed Forces Institute of Pathology, who also agreed that the lesion was a renal carcinoma He commented upon the similarity of the foam-type cell seen in this tumor to the granulomatous lesions known as pseudoxanthoma and felt that the definite

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RENAL CELL ADENOCARCINOMA IN A FIVE-YEAR-OLD GIRL WITH A REDUPLICATED COLLECTING SYSTEM AND ECTOPIC URETER OPENING INTO URETHRA

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From the Department of Urology, University Hospital, Baltimore, Md

Renal cell adenocarcinoma or, as it is commonly termed, hypernephroma, is a very rare neoplasm in childhood or adolescence Campbell[1] could find but four such cases in the American Tumor Registry Hempstead et al[2] reported 2 cases of hypernephroma in children, one of which was included in the 4 cases cited by Campbell and previously reported by Cathcart[3] In Hempstead's article there was a comment of a previously reported case of Hellstrom which showed marked regression in size after four days of preoperative irradiation, which would be most unusual for a true hypernephroma

Melicow[4] could find none of these tumors in infants or children in his review of 199 cases of renal tumors Johnson and Marshall[5] have recently reported 64 cases of kidney tumors seen over a 25-year period Of this group the great majority, 59, were Wilms' tumors They reported 3 cases of papillary adenocarcinoma, 2 cases of renal cell carcinoma

Although Johnson and Marshall separate papillary adenocarcinoma and renal cell carcinoma, all of the cases that they reported in this group presented with abdominal or flank masses, or had pyelographic deformities suggestive of tumor

Carlson[6] recently reported a case of hypernephroma in a 9-year-old boy and a careful review of the literature which disclosed 24 cases of this type of tumor in children He mentioned his knowledge of two additional cases by personal communication It would then appear that there have been approximately twenty six cases of this neoplasm seen and reported previously

Carlson's case presented with a large mass in the left upper abdomen and the surgical specimen weighed 1260 gm , apparently the largest as yet reported He listed, in tabular form, in his article the age, sex, etc , of all the previously reported cases that he found in a careful search of the literature, the youngest case being seen in an infant of 6½ months

We have recently seen such a case and believe that ours is unique in that no symptoms or clinical findings indicated the presence of a renal tumor It was discovered because of renal exploration made necessary for an entirely unrelated congenital abnormality

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CASE REPORT

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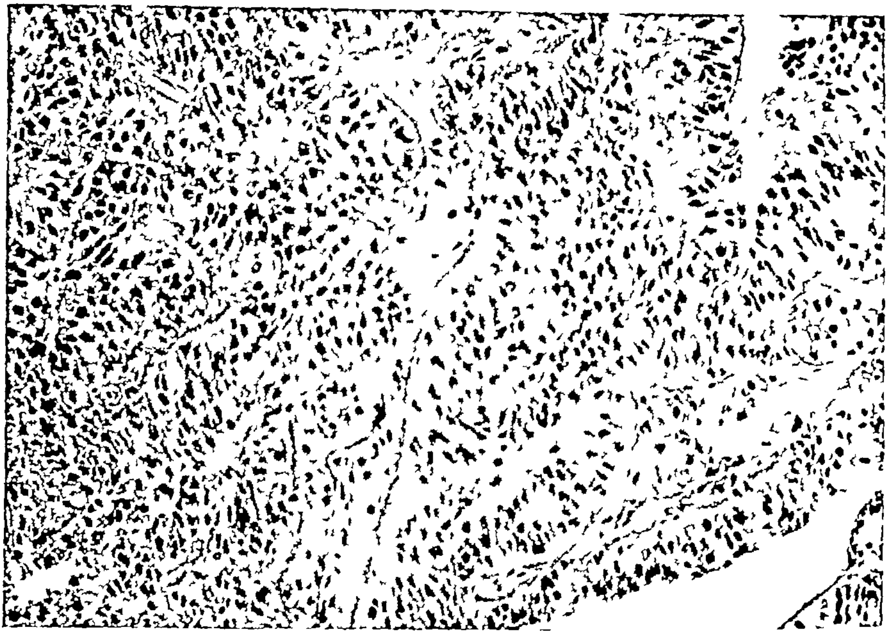

FIG 1

glands, lined by malignant cells, in this case clearly differentiated it to the class of renal cell carcinoma

Operation was undertaken again to perform nephrectomy of the lower renal segment The patient withstood the operation well Her postoperative course was complicated by a wound infection which delayed the convalescence but this slowly healed completely The pathological report of this specimen was negative for tumor It was not deemed helpful to give our patient radiation therapy because of the poor response of this type of tumor The child was discharged August 10, 1955 with a completely healed wound, in normal health and dry from the genitalia, both day and night Followup examination reveals that she is in robust health with no evidence of recurrence

DISCUSSION

The disputed pathogenesis of renal carcinoma, either from an original adenoma, or from the adrenal cell rests as suggested by Grawitz, is an interesting study and the works of Campbell,[7] Bothe,[8] Cabot and Middleton,[9] Trinkle,[10] Nicholson,[11] and Willis,[12] present the opposing views and the interested reader is referred to them

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If one accepts that renal adenomas are precursors of hypernephroma, it is interesting that our case presenting with such a small tumor had undergone malignant change Certainly, if one encounters a lesion resembling adenoma grossly, especially in the younger age group where its presence is most uncommon, it would seem that complete excision is warranted because of the unknown degree of histological change towards malignancy that may have occurred

SUMMARY

A case of renal cell adenocarcinoma has been presented in a 5-year-old patient The lesion did not produce a mass in the flank, pyelographic deformity, or gross hematuria It was discovered only because of renal exploration for a double collecting system with an ectopic ureter causing incontinence It is believed that this represents the twenty-seventh case reported of this tumor in childhood

Latrobe Building, Baltimore 2, Md (*J F H*)

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STUDIES IN THE PROPHYLAXIS OF URINARY TRACT CALCULI
I URINARY GLUCURONIDES

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Urine is often supersaturated with the crystalloid elements commonly found in urinary tract calculi [1] [2] Therapeutic regimens which decrease the urinary concentrations of these crystalloids have reduced the incidence of stone recurrence [3] [5] Undersaturation is the theoretical goal of such therapy

Approximately 34 per cent of urinary tract calculi contain apatite* and calcium oxalate, 19 per cent apatite, magnesium ammonium phosphate and occasionally calcium oxalate, and 33 per cent, chiefly calcium oxalate [6] Calcium, oxalate, and phosphate ($PO_4^{\equiv}$) are the three most frequently occurring constituents

Phosphorus exists in the urine in three different ionic forms, $H_2PO_4^-$, $HPO_4^=$, and $PO_4^{\equiv}$ The proportions in which these ions are present depend chiefly upon the pH of the urine In the usual acid urine of most individuals almost all of the phosphorus exists as H_2PO_4 and HPO_4 Small pH changes in the urine between the range of 5 0 and 7 0 effect relatively large changes in the amount of $PO_4^{\equiv}$ present [2] As the pH is lowered less PO_4J and more H_2PO_4 and HPO_4 are found The converse occurs with pH rises The phosphate concentration may also be lowered by decreasing the total phosphorus content of the urine

Endogenous oxalate excretion in the urine is not reduced by dietary limitation of oxalate Magnesium salts, administered orally, will substantially reduce endogenous oxalate in the urine A high oxalate diet may increase oxalate in the urine Therefore, if marked reduction of urinary oxalate is desired, a moderate dietary content of oxalate and the administration of magnesium salts are recommended [4]

The calcium *ion concentration of the urine may be reduced* by lowering calcium excretion and/or combining the free calcium ions with some other substance to form a soluble complex Citrate which appears normally in the urine is an

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* The apatites occurring most commonly in stones are the complex phosphates, carbonate apatite ($Ca_{10}(PO_4CO_3OH)_6(OH)_2$) and hydroxyl apatite ($Ca_{10}(PO_4)_6(OH)_2$)

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[6] Prien, E L Studies in urolithiasis II Relationship between pathogenesis structure and composition of calculi J Urol , 61 821–836, 1949

excellent complexing agent for calcium[7, 8] However, its excretion in the urine is limited and the known ways of creating increases in citrate excretion are not always reliable Moreover, citrate is often destroyed by bacterial action and many patients with calculus disease have urinary tract infections[9] Recently, interest has been aroused in the "complexing" of calcium with glucuronides, particularly conjugated glucuronides of salicylic acid[10] From the literature, it appears that with the concentrations of both single and conjugated glucuronides present in the urine, the increase in the solubility of calcium phosphates is, at best, about 16 per cent[11] This seems negligible in the face of the normal variations in urinary calcium and phosphorus of patients on a normal diet From theoretical aspects, any substance which would complex calcium to a high degree in the urine might do so similarly in other parts of the body, particularly bone This was noted when versene (a powerful chelating agent) was administered intravenously[12]

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STUDIES IN THE PROPHYLAXIS OF URINARY TRACT CALCULI
I URINARY GLUCURONIDES

MORTON BOGASH OTTO ROSENTHAL AND JOHN J MURPHY

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RESULTS

1 *Glucuronide excretion* (*table 1*) The average glucuronide excretion in the control specimens was 642 mg for 24 hours On the acetysalicylic acid regimen the average value was 1204 mg /24 hours with the average increase in glucuronide excretion being 539 mg Glucuronolactone plus aspirin in the regimen described yielded an average glucuronide level of 1441 mg with an average rise of 800 mg Glucuronolactone alone produced an average rise of 499 mg with an average total excretion of 1141 mg The total glucuronide excretion was increased almost equally by acetylsalicylic acid and glucuronolactone given singly and to a higher level when these substances were taken together However, their effect together was less than additive

2 *Calcium* (*table 1*) All specimens lost calcium following equilibration with tri-calcium phosphate No constant relationship was demonstrated between the amount of calcium lost and the calcium concentration in the urine prior to equilibration A trend was noted in that the urines with higher calcium concentrations tended to lose larger amounts of calcium following equilibration

3 *Phosphorus* (*table 1*) Changes in phosphorus following equilibration were greater than 5 per cent of the total phosphorus in three specimens of which all lost phosphorus, greater than 3 per cent in nine specimens of which one gained and eight lost phosphorus and greater than 1 5 per cent in 25 specimens of which eight gained and 17 lost phosphorus Forty specimens were analyzed

DISCUSSION

The experiments described above may indicate that the calcium phosphates are not always in a supersaturated state in the filtered urine of normal individuals since phosphate did not always precipitate out when the urine was equilibrated with tri-calcium phosphate However, it is possible that the loss of phosphorus involved in the precipitation of the calcium phosphates may have been too small to have been measured considering the limitations of the method and the total urinary phosphorus

It should be borne in mind that the initial filtration of urine removed calcium phosphate (probably as $CaHPO_4$ as shown by Andrews, and others)[13] Unfortunately the total calcium and phosphorus prior to initial filtration were not determined Therefore, the amounts of these substances removed by the *initial* filtration are unknown If undersaturation were present only negligible amounts of, or none of these substances would be removed by the initial filtration

The urine is apparently supersaturated with some calcium salts since a measurable amount of calcium is always lost following equilibration Urinary volume, pH and glucuronide concentration varied independently of each other and it was difficult to note any relationship between any one of these factors and the absolute calcium concentration after equilibration or the *calcium lost through* equilibration However, it appeared roughly as though some slight solubilization of calcium salts had been affected by high urinary glucuronide concentrations Despite this it may be stated unequivocally that elevated glucuronide levels

TABLE 1

Patient		Controls				ASA		ASA + Gluc.		Gluc.	
No 1 J J M	pH before equil	5 8	5 8	5 7	5 9	5 5	6 3	5 8	5 5	5 6	5 5
	Volume (ml)	1810	1450	2020	985	1160	2055	1245	1850	1390	2020
	P before equil (u gm /ml)	517	604	178	1081	1128	489	880	666	852	500
	Δ P after equil (u gm /ml)	−10	+11	−3 5	−12	−23	−21	−11	−11	−8	+7
	Ca before equil (u gm /ml)	76	86	37	148	146	86	123	136	113	46
	ΔCa after equil (u gm /ml)	−3 0	−32 5	−4 2	−45	−28	−32	−35	−31	−40	−18
	Glucuronides (u gm /ml)	460	368	144	660	1490	668	1370	768	1012	543
No 2 W G	pH before equil	6 0	6 7	5 9		5 5	5 84	6 4	5 1	5 4	5 7
	Volume (ml)	978	1150	1080		1160	1880	1510	960	920	1380
	P before equil (u gm /ml)	937	919	486		653	408	837	1101	1310	659
	ΔP after equil (u gm /ml)	+32	−22	+7		−8	−4	−37	+10	+13	−3
	Ca before equil (u gm /ml)	133	131	119		132	103	188 5	168	220	125 6
	ΔCa after equil (u gm /ml)	−48	−51	−22 7		−35 2	−35 3	−58 6	−13 7	−61 5	−48 7
	Glucuronides (u gm /ml)	677	724	695		823	510	768	1260	1143	479
No 3 M B	pH before equil	5 4	5 4	6 2	5 9	6 1	5 5	5 4	5 3	5 5	4 9
	Volume (ml)	630	530	3120	1800	1728	1839	1015	1135	1910	1760
	P before equil (u gm /ml)	916	1164	200	390	323	475	955	870	561	460
	ΔP after equil (u gm /ml)	+19	−14	−3 5	+7	−8	+7	0	0	−4	+3
	Ca before equil (u gm /ml)	154	158	53 5	70 6	151	87 8	165	130	117	75 4
	ΔCa after equil (u gm /ml)	−38 2	−37	−30	−6 8	−49 5	−16	−31 6	−19 6	−44 2	−16 9
	Glucuronides (u gm /ml)	790	665	163	266	504	567	1310	1240	575	516
No 4 W O	pH before equil	6 1	5 9			6 6	5 9	5 6	5 9	6 5	6 1
	Volume (ml)	1360	1070			1830	1220	1779	1405	1220	1650
	P before equil (u gm /m)	745	1286			795	902	645	983	1028	759
	ΔP after equil (u gm /ml)	−25	−58			−39	−18	−7	−28	−8	−18
	Ca before equil (u gm /ml)	222	259			134	172	196	228	174	207
	ΔCa after equil (u gm /ml)	−67	−130			−81 4	−52	−47 2	−69 5	−39 3	−54
	Glucuronides (u gm /ml)	523	823			748	1095	1040	1030	1116	945

P = phosphorus
Ca = calcium
ASA = acetylsalicylic acid
ASA + Gluc = acetylsalicylic acid + glucuronolactone
Gluc = glucuronolactone

5 Glucuronolactone, 5 gm per day in divided doses was then administered for three days and urine collected for the last two days of this program

METHODS

Each 24-hour specimen was treated in a similar fashion The specimens were refrigerated during collection An aliquot was suction filtered through Watman No 50 paper Some of this aliquot was removed and urinary pH, calcium, phosphorus and glucuronide determined One hundred ml was taken and mechanically shaken for four hours at 25°C with one gram of powdered tri-calcium phosphate (Merck reagent) The aliquot was then suction filtered as above and the pH, total calcium and phosphorus of the filtrate were determined The Beckman model G-pH meter was used to measure urinary pH Calcium was determined by modification of the Sobel method[14] Phosphorus was determined by a modification of the Fiske-Subbarrow method Glucuronides were determined by a modification of the method of De Frates[15] [16]

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[14] Sobel, A E and Kaye, I A Estimation of submicroquantities of calcium Indus & Eng Chem , Analytical Ed , 12 118, 1940

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A STUDY OF THE PERISTALTIC CONDUCTION MECHANISM IN THE CANINE URETER

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and WERNER P SCHMANDT†

From the Department of Surgery and the Department of Physiology, Washington University School of Medicine, St Louis, Mo

Despite many investigations of ureteral peristalsis,[1] [2] the nature of its transmission along the ureter is poorly understood This study undertakes to define accurately the electrical properties of peristaltic conduction and to investigate the factors affecting them in an attempt to learn more of the mechanism responsible for propagation of the contraction wave through ureteral smooth muscle

METHODS

All experiments were conducted upon ureters in situ to assure good oxygenation Adult mongrel dogs of both sexes were anesthetized by intravenous injection of sodium pentobarbital (0 03 gm /kilo) and a cystostomy was performed to permit easy insertion of an electrode assembly into an ureteral lumen A multichanneled modified Offner dynograph recorded the action potentials of peristaltic waves from the intraluminal electrodes of fine silver wire (01 inch diameter, fig 1) All electrode leads were insulated by stretching polyethylene tubing (04 inch diameter) over them A small, distensible rubber balloon attached to polyethylene tubing (04 inch diameter) was inserted into the upper ureter through an opening in the renal pelvis Peristaltic waves were stimulated when desired by brief distension of the balloon

The effect of different temperatures upon ureteral conduction was studied by placing Ringer's solutions of varying temperatures into a peritoneal recess constructed about a segment of the ureter containing two or three electrodes Temperature of the fluid bathing the exposed ureteral segment was observed and correlated with the action potentials recorded from the electrodes placed in the ureter contained in the peritoneal pocket The lag of temperature change in the ureteral wall compared to that of the fluid about it was measured in two experiments by using a needle thermocouple inserted into the ureteral muscle Conductional effects of drugs were studied by placing solutions of them in peritoneal recesses, by intravenous administrations and by their injection into the ureteral wall Conduction of waves in ureters having healed anastomoses was studied similarly[3]

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[1] Gruber, C M The autonomic innervation of the genito urinary system Physiol Rev , 13 497–609, 1933

[2] Butcher H R , Jr and Sleator, W , Jr Action potentials and pressure changes in ureteral peristaltic waves Am J Physiol , 180 261–276, 1955

[3] Idem The effects of ureteral anastomosis upon conduction of peristaltic waves An electro ureterographic study J Urol 75 650–658, 1956

did not render the urine of normal individuals undersaturated with calcium salts

Failure of elevated urinary glucuronide concentrations to render urine undersaturated with calcium salts is not surprising This is in agreement with reports indicating that only slight solubilization of calcium salts can be expected with the urinary glucuronide concentrations attainable with salicylates and/or glucuronolactone [11] [17] Despite this, there is evidence that salicylate therapy may reduce stone recurrences through another mechanism All calculi contain crystalloids and an organic matrix, a mucoprotein, mucopolysaccharide compound [18] A material with staining properties somewhat similar to matrix appears in increased amounts in the renal connective tissue of patients with urinary tract calculi [18] [19] The administration of antiinflammatory drugs (among them salicylates) reduces the quantity of this matrix-like material in the kidneys of stone formers [19] A reduced rate of stone recurrence has been reported in patients so treated The matrix is probably present in colloidal form in urine Dispersion as well as reduction of the quantity of matrix might prevent stone growth Therapy directed at both the matrix and crystalloids, simultaneously, may be more effective than a unilateral approach

CONCLUSIONS

Urine is almost always supersaturated with calcium salts

The total glucuronide excretion in the urine is increased almost equally by acetylsalicylic acid and glucuronolactone given singly and to a higher level when these substances are taken together Their effect together is less than additive.

Elevated urinary glucuronide levels may cause some solubilization of calcium salts in the urine However, the elevated glucuronic levels attained with the recommended dosages of acetylsalicylic acid and/or glucuronolactone do not render the urine undersaturated with calcium salts

Equilibration techniques may be useful in screening these programs of stone prophylaxis designed to produce undersaturation of the urine with the salts commonly found in calculi

The authors wish to express their appreciation for the technical assistance of Mrs Muriel Asbornsen in performing the various chemical determinations

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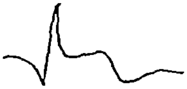
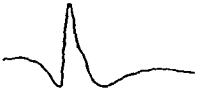
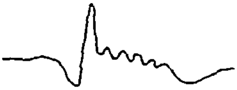
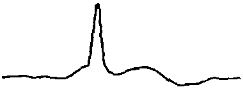
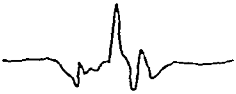
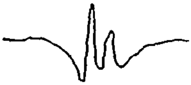
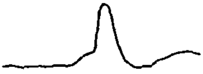
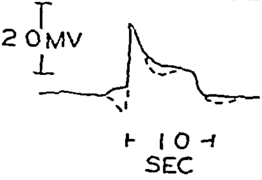
[19] Baker, R and Connelly, J P Bilateral and recurrent renal calculi Evidence indicating renal collagen abnormality and results of salicylate therapy J A.M.A 160 1106-1110, 1956

Table 1

This table shows traced examples of canine peristaltic action potentials recorded under the circumstances tabulated to the right of each wave No 7 is an example of an action potential recorded intracellularly from cardiac pacemaker cells, reproduced from West et al [6] The postulated true action potential shape of canine ureteral waves is shown below The dotted portion of this figure indicates the areas of the recorded action potential caused by artefacts of volume conductor recording The prepotential shown in this wave probably is present only at the sites of origin of ureteral action potentials and not in conducted waves

	TISSUE	POSITION OF THE ELECTRODE	TEMPERATURE	WAVE INTERVAL	RECORDED ACTION POTENTIAL
1	Ureter	Intraluminal away from site of wave origin	37° C	5 plus seconds	
2	Ureter	As in (1)	37° C	1 second	
3	Ureter	As in (1)	28° C	5 plus seconds	
4	Ureter	Intraluminal at site of wave origin	37° C	5 plus seconds	
5	Ureter	In lumen of a healed anastomosis	37° C	5 plus seconds	
6	Ureter	Intraluminal near healed anastomosis	37° C	5 plus seconds	
7	Cardiac	Intracellular pacemaker cells	37° C	0 6 seconds	
8	Ureter	Postulated true shape of the action potential at 37° C after a wave interval of 5 or more seconds			

RESULTS

1 *Normal peristaltic action potentials* The action potential of a single peristaltic wave consisted of a spike followed by partial repolarization, a plateau and completion of repolarization (table 1) When the peristaltic wave originated in the ureter away from an electrode, its action potential possessed an approach artefact (table 1, 1) When a wave arose at an electrode, no approach artefact was seen (fig 1, 4) (Additional evidence that the wave arose at a given electrode was its simultaneous appearance at equidistant electrodes above and below the electrode of origin) In most such waves, a small slow rise of negativity (prepotential) was recorded before the onset of the action potential spike (table 1, 4)

2 *Postperistaltic interval of reduced wave velocity* If one wave follows another within a few seconds, the speed of the second wave is less than the first This postperistaltic interval of reduced velocity lasts typically for about three seconds and occasionally as long as six seconds During the interval of reduced velocity, the voltage time contour of the action potential of the peristaltic wave is abnormal (fig 2) In the earlier part of this period, that is, just after passage of the distension refractory period (0 5–0 6 second after the peristaltic wave) there is a reduction in the total duration of the action potential, a broadening of the negative peak phase with little change in voltage and no separation of re-

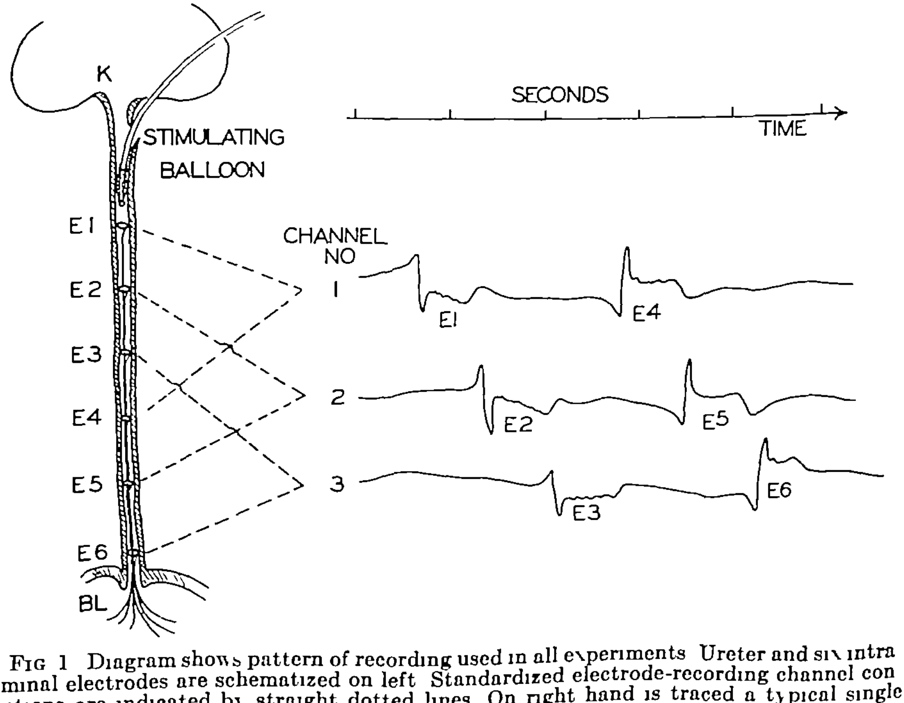


FIG 1 Diagram shows pattern of recording used in all experiments Ureter and six intraluminal electrodes are schematized on left Standardized electrode-recording channel connections are indicated by straight dotted lines On right hand is traced a typical single peristaltic action potential as it passed successive electrodes 1 through 6

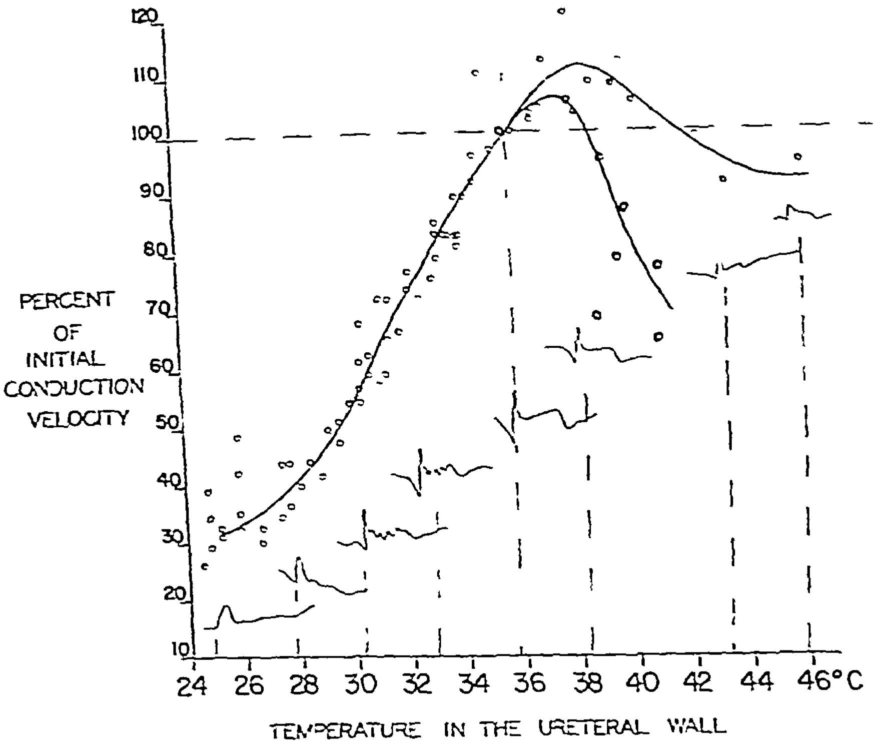


Fig. 3 Effect of different temperatures in ureteral wall upon conduction velocity and action potential shape is shown in graph Lower line and accompanying heavy circles above 36 C illustrate slower velocity of waves occurring during reduction of temperature from one sufficiently high to produce conductional block

Moderate elevation of the temperature of the ureteral environment above 37°C shortened the duration of the plateau increased slightly the conduction velocity and increased the spontaneous activity of the ureter Beyond 41°C velocity fell with temperature increase and finally at 45°–46°C temperatures were reached which produced conductional block A return of temperature to within physiologic limits was followed by a return of conduction if heating beyond the point of block had not been excessive or prolonged When conduction returned with cooling slower velocities a decrease in slope of the action potential spikes and a lessening of their voltages were frequently noted below those observed at specific temperatures during heating These changes were qualitatively similar to those observed when the temperature was elevated from a prolonged state of cooling sufficient to block conduction

4 *The changes in action potential shapes associated with healed ureteral anastomoses with and without nephrectomy at the time of ureteral transection and anastomosis* Analysis of the effect of ureteral transection and anastomosis upon subsequent conduction of peristalsis has been presented[2] If wave conduction was delayed in the absence of significant stricture at a healed anastomosis the duration of delay roughly correlated with the degree of hydronephrosis found at

polarization into two phases by a plateau Previous investigation[2] has shown that these action potential and velocity changes are associated with lessening of the strength of ureteral contraction The direction of conduction along the ureter does not influence these changes However, the effects of an initial wave upon velocity and action potential shape persist after a second wave when a third one is stimulated within 6-8 seconds of the initial one (fig 2)

3 *The effect of environmental temperature upon canine ureteral peristaltic action potentials* Moderate lowering of the temperature of a segment of canine ureter by the application of cold mammalian Ringer's solution to it decreased the velocity of conduction, lowered the voltage of the plateau of the action potential and transformed it into oscillations (fig 3) When the temperature of the solution immediately adjacent to the segment of ureter reached 22° to 24°C, conduction through it ceased At temperatures just above that required to produce block, the velocity was the least and the plateau frequently not observed If a segment cooled briefly just to the point of block was then warmed, conduction through it again occurred at velocities and with wave shapes similar to those seen as the temperature was lowered If, however, cooling was severe or prolonged prior to subsequent elevation of the temperature, the action potentials showed a loss of voltage, a broadening of its spike (due to slowing of both depolarization and repolarization), a loss of the plateau and a slower velocity of conduction than was present at a given temperature during stepwise cooling

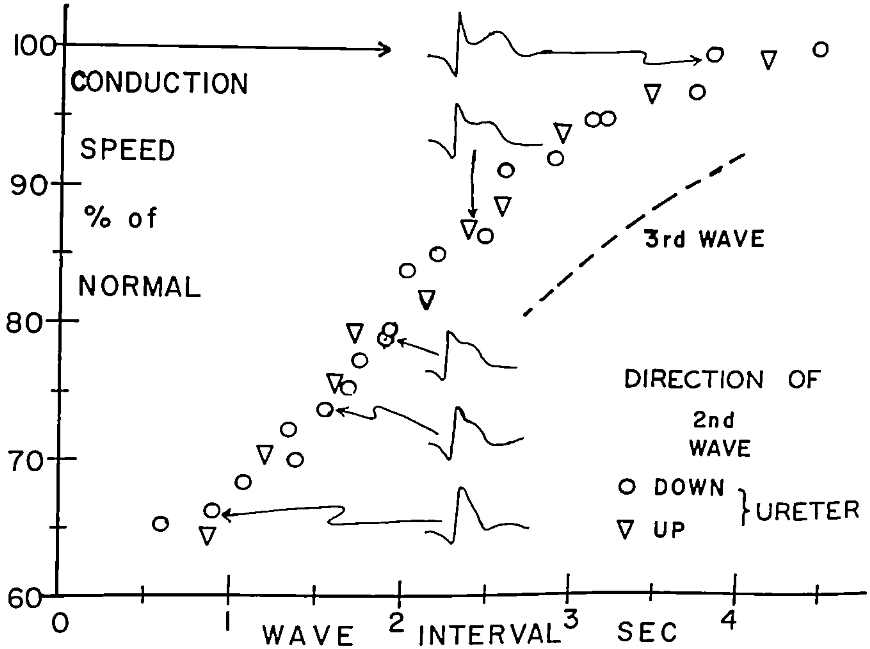


FIG 2 Graph shows relationship of interperistaltic wave interval, conduction velocity, and action potential shape Dotted line labeled "third wave" indicates further velocity decrement of a wave appearing four seconds or less after plotted second waves No differences were found between waves conducting up ureter and those moving down it

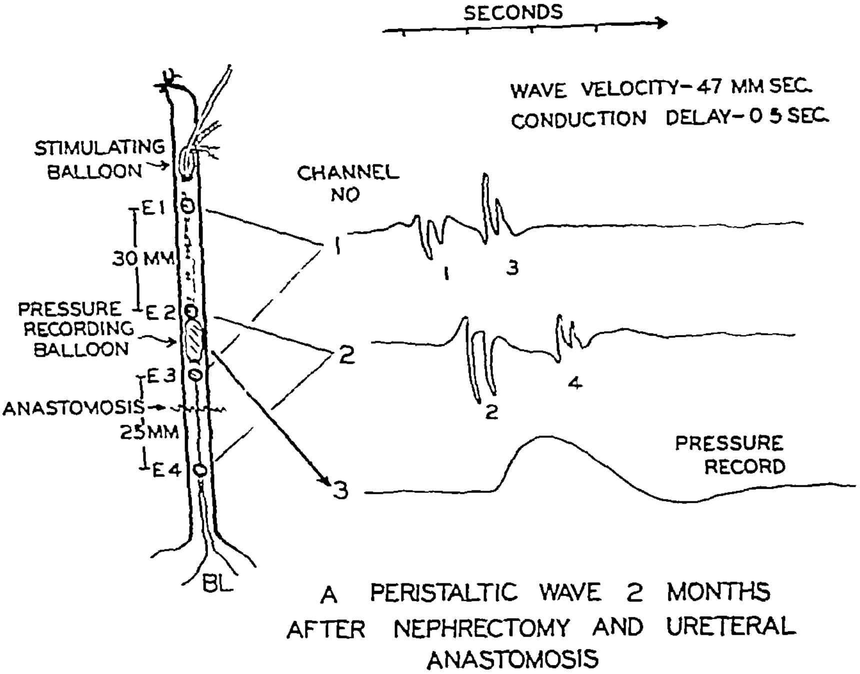

SECONDS
WAVE VELOCITY-47 MM SEC.
CONDUCTION DELAY-0 5 SEC.
STIMULATING BALLOON
CHANNEL NO
E1
30 MM
PRESSURE RECORDING BALLOON
E2
E3
ANASTOMOSIS
25MM
E4
BL
1
2
3
1
3
2
4
PRESSURE RECORD
A PERISTALTIC WAVE 2 MONTHS AFTER NEPHRECTOMY AND URETERAL ANASTOMOSIS

FIG 5 Schematic drawing on left illustrates conditions of experiment Kidney was removed, ureter transected and anastomosed 2 months before ureteral action potentials were stimulated and recorded

Action potential of a single peristaltic wave is shown as it was recorded from four electrodes connected to channels 1 and 2 At all electrodes recording showed complete replacement of plateau of action potential by a secondary spike In some waves plateau was replaced by 2 to 3 secondary spikes Channel 3 indicates contraction wave as it passed recording balloon between electrodes 2 and 3, and shows wave to be a single one despite presence of secondary spikes Pressure changes in water-filled balloon were recorded with use of a Sanborn electromanometer

peristalsis but did not alter significantly the shape of the resulting action potentials Its effect on the velocity of peristalsis consisted of a shortening of the period of reduced wave velocity In other words, during the high frequency peristalsis caused by histamine, the slowing of velocity caused by the recent passage of a preceding wave was less than that expected in the ureter being studied However, no restoration of conductivity across anastomotic ureteral scars followed its application to them

The administration of pyribenzamine (tripelennamine citrate) or benadryl (diphenhydramine hydrochloride) decreased the voltage and broadened the peak phase of both the action potentials of histamine stimulation and those initiated by distension until they no longer were recordable (fig 6) The antihistaminic drugs caused changes similar to those seen with fatigue or injury of the ureter These findings suggest that these drugs may prove of value in relief of ureteral pain Temporary relief of pain followed the use of benadryl in three of four patients with ureteral colic the time of study The action potentials conducted through the anastomoses and recorded from electrodes placed in the anastomotic lumen showed arrival of the action potential with an approach artefact, an iso-electric period corresponding to the duration of delay in action potential conduction and a "departure" spike preceded by a prepotential and followed by an abnormal period of repolarization (fig 4) The latter consisted of marked oscillations or secondary spikes in place of the plateau of the action potentials These plateau abnormalities were recorded in or adjacent to the ureteral scar in most instances and in all parts of a right ureter studied two months after right nephrectomy, ureteral transection and anastomosis (fig 5)

5 *The absence of effect of drugs upon action potential shape* Nicotine, curare, hexamethonium chloride, xylocaine, prostigmine, acetylcholine with and without eserine, atropine, epinephrine and regitine produced no change in velocity of conduction or shapes of the peristaltic action potentials (table 2) Histamine, locally or systemically administered, increased the wave velocity and the frequency of

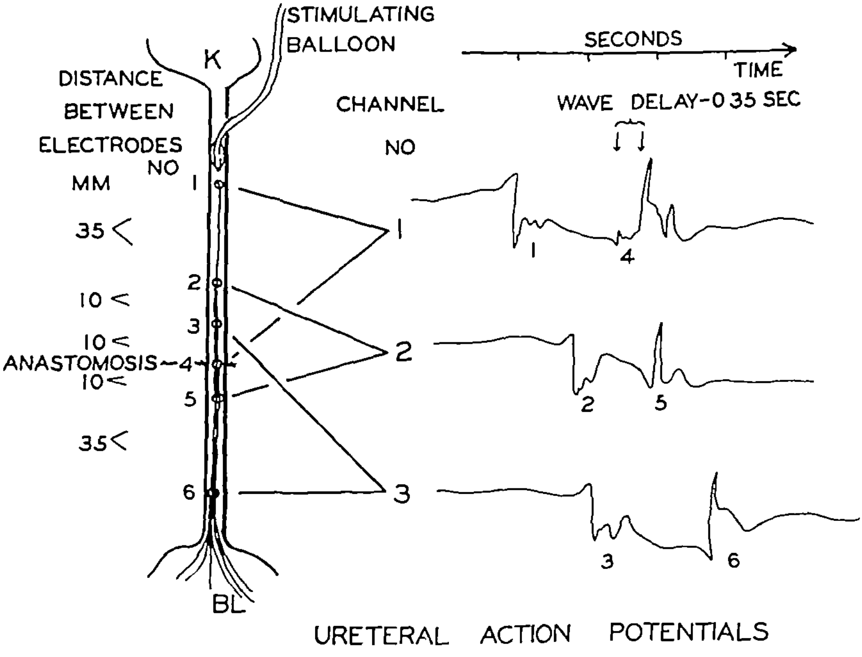
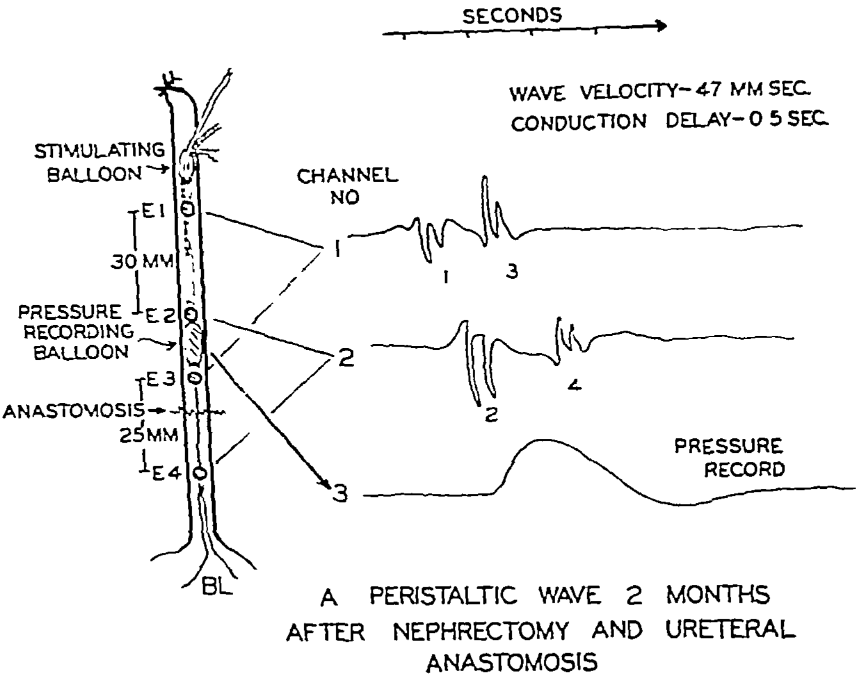


FIG 4 Action potential recording of a single stimulated peristaltic wave propagating down ureter and through anastomotic scar is traced on right Time scale and delay in conduction of the wave at anastomosis are shown above Electrode No 4 was placed in ureteral lumen at anastomotic site Interelectrode distances are shown in millimeters on left Departure spike at electrode 4 was preceded by a prepotential and followed by near complete replacement of plateau by a secondary spike Similar but less complete change in plateau of action potentials at electrodes 3 and 5 was observed These electrodes were only 10 millimeters from the anastomotic scar



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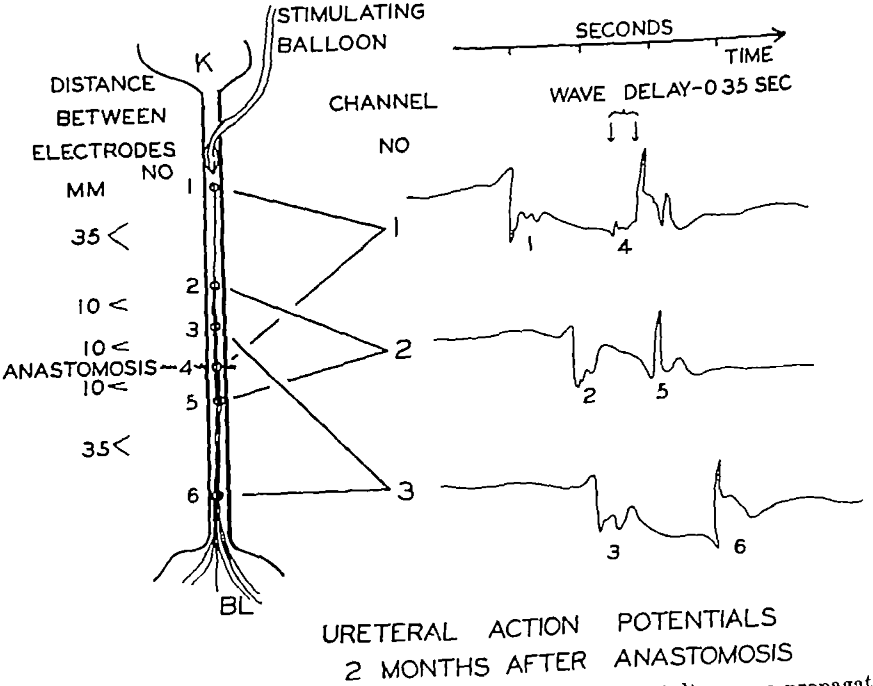

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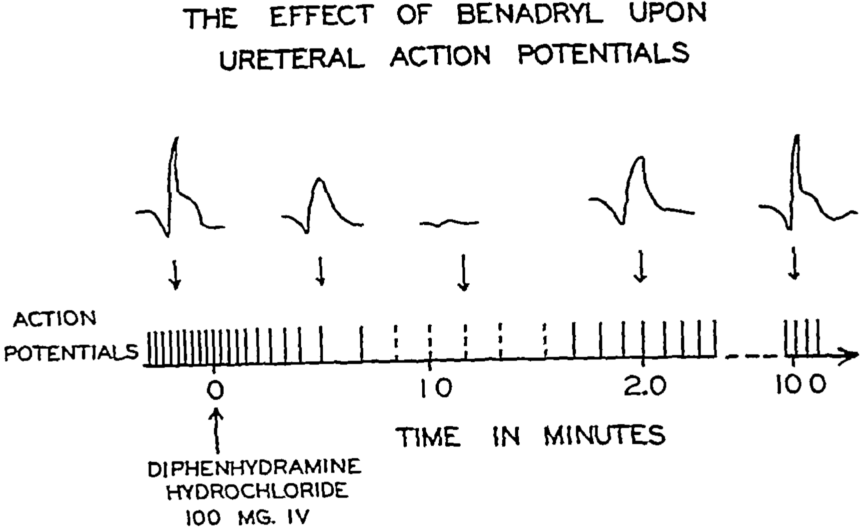

FIG 6 This figure summarizes an experiment in which 100 mg of benadryl (diphenhydramine hydrochloride) was given intravenously during active ureteral peristalsis Effect upon shape of action potentials is shown by traced examples above time scale Each short line perpendicular to time scale represents a peristaltic wave Ones appearing about one minute after the drug administration have been dotted because some of these action potentials were so depressed as to make their presence doubtful

also seen in other conducting tissues[4, 5] A similar slow low voltage prepotential has been recorded intracellularly from cardiac muscle in or near the pacemaker (table 1, 7),[6] and from nodes of myelinated nerve fiber stimulated by long duration shock near threshold strength It appears that a prepotential is common to tissue about to develop an action potential spike and is recordable if not obliterated by an approach artefact at the recording electrode It accompanies activation in tissues capable of "self-initiation" of impulses The fact that the ureter is capable of stimulation by other than electrical or synaptic mechanisms is in harmony with the presence of a prepotential

The cause of the plateau during repolarization of the action potential, what is responsible for its oscillation with cooling, its disappearance with fatigue and its replacement with a secondary spike or spikes adjacent to healed ureteral scars remain unknown If the causes of these reproducible changes in the action potential shape were adequately explained, the mechanism of ureteral conduction would likely be understood

The mechanism of conduction of ureteral peristalsis has been debated since

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[4] Hutter, O F and Trantwein, W Vagal and sympathetic effects on the pacemaker fibers in the sinus venosus of the heart J Gen Physiol, 39 715-733, 1956

[5] Jenerick, H P The relations between prepotential resting potential, and latent period in frog muscle fibers J Gen Physiol, 39 773-787, 1956

[6] West T C Falk G and Cervoni, P Drug alteration of transmembrane potentials in atrial pacemaker cells J Pharm and Exper Therap, 117 245-252 1956

[7] Engelmann, T W Zur Physiologie des Ureter Pfluger's Arch f d ges Physiol, 2 243-293 1869

TABLE 2 *The effects of drugs upon ureteral activity*

Solutions of Drugs (37 C)	Method of Application				Frequency	Action Potentials
	Injection into ureteral wall	In peritoneal recess (50 cc volume)	I V	I A.		
Epinephrine 1 1000 solution	1 cc	+	2 cc	2 cc	No effect	No effect
Regitine 0 5 1000 solution	—	—	15 cc		No effect	No effect
Acetylcholine 1 100 solution (alone and after eserine)	1 cc	+	5 cc	5 cc	No effect	No effect
Eserine 1 1000 solution	—	+	2 cc	—	No effect	No effect
Atropine 1–2 cc 1 100 solution	—	+	—	—	No effect	No effect
Nicotine 1–2 cc 1 100 solution	—	+	—	—	No effect	No effect
d - Tubocurarine 1 mg /cc	1 cc	—	5 mg /kilo	—	No effect	No effect
Hexamethonium chloride 40 mg / cc	1 cc	+	—	—	No effect	No effect
Histamine hydrochloride 1 10,000 solution	—	+	10 cc		Increase	No effect
Pyribenzamine 10 mg /cc	—	+	8–10 cc	8–10 cc	No effect or decrease	"Fatigue effect"*
Benadryl 10 mg / cc		+	10 cc		No effect or decrease	"Fatigue effect"

* By "fatigue effect" is meant the disappearance of the plateau of the action potentials, the reduction of their voltage and the broadening of their peak phase Such changes also are seen with the "fatigue" resulting from hours of stimulation and manipulation of ureter and with death of the animal

DISCUSSION

The shape and conduction velocity of canine ureteral action potentials have been found to be altered primarily by physical and temporal factors, namely 1) the site of origin in relation to the recording electrode, 2) the time since the preceding peristaltic wave, 3) the temperature of the ureteral wall and 4) the presence of healed ureteral anastomosis These factors are stressed in this study, because of the drugs tested, only histamine and antihistaminic drugs had an effect upon ureteral peristalsis

The prepotential recorded when an action potential arose at an electrode is through an area of ureter whose lumen was moderately distended with an obturator which prevented appreciable narrowing or distortion of it. Also, delays in conduction of a peristaltic wave of greater than one second in a healed ureteral anastomosis suggest that distortion incident to the wave's arrival likely has disappeared before the onset of the departure phase of the wave.

The two theories of ureteral smooth muscle conduction which seem most plausible at the moment are 1) the direct firing of a cell by the electrical breakdown of its neighbor, and 2) the release by a contracting cell of some substance which activates its neighbor. Proesser et al[3] favor the former hypothesis. The evidence for either theory is as yet inconclusive. However, further study may show histamine or some histamine-like substance to be the agent responsible for conduction in ureteral smooth muscle.

SUMMARY

The variations in the shape of canine ureteral action potentials and the conditions resulting in these changes have been studied. Physical and temporal factors affecting action potential shape in canine ureters were:

The site of origin of the wave in relation to the recording electrode (table 1, 4)

The wave interval when below 4–6 seconds (fig. 2)

The temperature of the ureteral wall (fig. 3)

The presence of an anastomotic scar at or near the recording electrode (figs. 4, 5)

Of the drugs studied (table 2) only histamine and antihistamine drugs effect change in action potential shape or conduction velocity. Histamine increased the spontaneous activity of the ureter, and decreased the effect of the passage of preceding waves upon the velocity of subsequent ones, but did not appreciably alter action potential shape. Pyribenzamine and benadryl decreased the voltage and broadened the peak phase of both the action potentials of histamine stimulation and those stimulated by distension (fig. 6)

The mechanism of peristaltic wave conduction may be the release of some histamine-like substance by a contracting cell which stimulates contraction of neighboring cells.

[3] Proesser, C. L., Smith, C. E. and Melton, C. E. Conduction of action potentials in the ureter of the rat. Am. J. Physiol., 181: 651–660, 1955.

Engelmann[7] concluded in 1869 that peristaltic conduction is myogenic in origin and that neural stimuli are not initiating factors The mechanisms of conduction that deserve consideration are

1 A neural network responsible for initiating conduction of smooth muscle contraction

2 Smooth muscle protoplasmic bridges resulting in a syncitium allowing conduction

3 Conduction by mechanical distortion of the neighboring cell by the contracting one

4 Ephaptic conduction or the direct firing of a cell by the electrical breakdown of its neighbor

5 The release of an unknown substance by a contracting cell which activates its neighbor

In this study, the factors effecting the conduction of peristalsis were found to be primarily physical ones, drugs having no effect upon the shape of peristaltic action potentials Histamine appeared to alter conduction in ureteral smooth muscle, as evidenced by the high frequency response of the ureter, a slight increase in velocity and a shortening of the period of reduced wave velocity but it did not change the shape of the action potential The absence of effect upon conduction velocity and action potential shape by cholinergic and adrenergic drugs, and the transitory nature of blocking by anesthetic agents[2] suggest that neural elements are not responsible for conduction If a neuromuscular synapse were involved in conduction of peristalsis, acetylcholine should effect it as it does the neuromuscular synapse or motor end-place of skeletal muscle The application of this drug in doses high enough to cause ventricular fibrillation in the dog did not effect peristaltic conduction Also, previous study[2] has shown no preference in the direction of wave propagation in canine ureters In order for a neural network to be involved in ureteral conduction a "double system" of nerves needs be postulated since in all known instances, the receptor and effector ends of nerves differ Finally, the paucity of ganglion cells and discernible nerve fibers among the smooth muscle cells of the ureter further gainsay the importance of neural factors in ureteral conduction

The postulation of a smooth muscle syncitium as the mechanism by which an action potential is conducted along the ureter is not warranted because protoplasmic bridges between smooth muscle cells have not been identified by electron microscopy [8] Indeed, the general concept of syncitial conduction needs now be questioned since electron microscopy gives evidence that the intercolated discs of heart muscle are really cell boundaries If protoplasmic bridges are present between the smooth muscle cells of the ureter, they are so small that electrical resistance would be great and conduction across them difficult

Mechanical distortion by a contracting cell of its neighbor should be seriously considered as a possible mechanism of ureteral smooth muscle conduction since the initiation of ureteral contraction is best accomplished by distension [2] However, in a previous study,[2] conduction of peristalsis was occasionally recorded

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[8] Weiss, J Unpublished data

Boiling for thirty minutes in this manner fairly consistently yielded smooth surfaced pieces of sponge measuring 2 mm in thickness Approximation was accomplished with a continuous 000 plain catgut suture The wound was closed in layers without drainage Penicillin and streptomycin were administered for 3 days postoperatively

The animals were sacrificed by bleeding at 12 weeks Urine for bacteriologic study was obtained by needle aspiration of the intact bladders prior to their removal The fresh specimens were photographed and then fixed in formalin Representative sections were cut after fixation and stained with hematoxylin and eosin for microscopic study

RESULTS

Experiments on six dogs were done One animal died on the third postoperative day due to an inadvertent parenteral overload of potassium A second animal died on the fifth postoperative day due to peritonitis and wound evisceration Four animals survived the period of the experiment with no untoward effects Minimal local inflammatory reaction about the site of the polyvinyl sponge implant was evident grossly The external surface of the bladders revealed only a well healed scar (fig 1, *A*) In two dogs there was some adherent

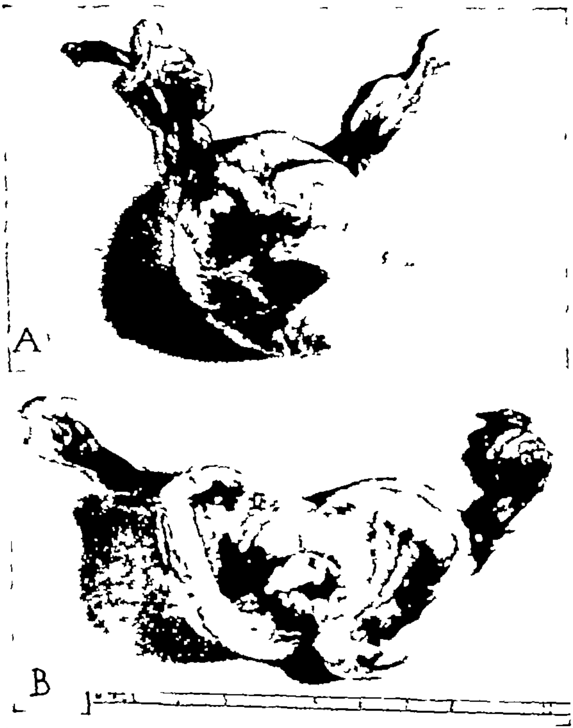

FIG 1 *A*, external surface of bladder *B*, luminal surface of bladder shows polyvinyl sponge partially extruded

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THE USE OF POLYVINYL SPONGE FOR EXPERIMENTAL CYSTOPLASTY

HAROLD G KUDISH

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Nonabsorbable foreign materials have occasionally been useful in the surgical reconstruction of various organs and body structures Tantalum, vitallium, stainless steel, polyethylene and methyl-methacrylate have replaced living tissue to fill defects or correct deformities The limitation of foreign materials is well recognized Foremost among these, and common to all in widespread use, is the failure of union with the surrounding living tissue In specific circumstances this characteristic is not a limitation but rather an asset In others it is more or less a handicap, while in still others it constitutes a major objection to the use of foreign materials It is apparent, therefore, that stable and biologically inert, nonabsorbable materials, which become a part of the structure of the living tissue, would be extremely important in surgery

Polyvinyl sponge is made from polyvinyl alcohol by a special process wherein the polyvinyl alcohol is foamed and then hardened with formaldehyde Sponges of uniform texture and quality are commercially available for cleaning purposes They are available for medical use under the name of ivalon *

The color of pure polyvinyl sponge is white The cut surface resembles a slice of white bread, but the texture can be varied considerably during the manufacturing process Dry polyvinyl sponge is hard and rigid, whereas moist sponge is resilient, soft, and possesses great tensile strength The density is approximately 0 05 The most prominent characteristic of polyvinyl sponge is its great affinity for water Temperatures up to 120 degrees C have no effect on it Boiling in water for the first time produces slight shrinkage At ordinary temperatures polyvinyl sponge is inert to most chemicals It is not affected by strong or weak acids or alkalies, organic solvents, formaldehyde or glycerols Sterilization is easily accomplished by boiling for 30 minutes

Accurate molding is very simple Any deformity created during the boiling process is maintained when the sponge is cooled The sponge is shaped to a rough approximation of the desired shape prior to boiling because excessive compression will impede the ingrowth of living tissue

METHODS

Mongrel dogs, weighing 12 to 25 kg , were anesthetized with intravenous nembutal and the bladder exposed through a midline incision A roughly circular full-thickness segment of bladder wall approximately 5 cm in diameter was resected The defect thus created was replaced with compressed polyvinyl sponge of comparable size Compression was accomplished by tightly wrapping a piece of moist sponge, 4 mm in thickness, around a steel cylinder with gauze bandage

Accepted for publication April 18, 1957

* Clay-Adams, Incorporated

Boiling for thirty minutes in this manner fairly consistently yielded smooth surfaced pieces of sponge measuring 2 mm in thickness Approximation was accomplished with a continuous 000 plain catgut suture The wound was closed in layers without drainage Penicillin and streptomycin were administered for 3 days postoperatively

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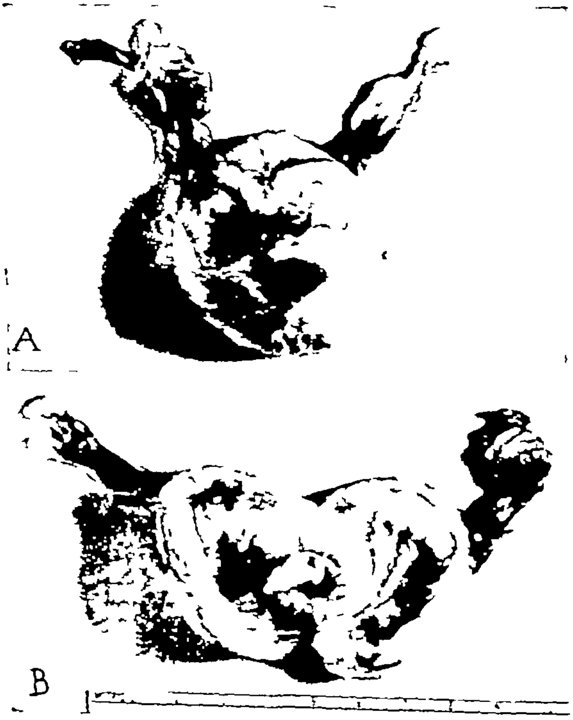

FIG 1 *A*, external surface of bladder *B* luminal surface of bladder shows polyvinyl sponge partially extruded

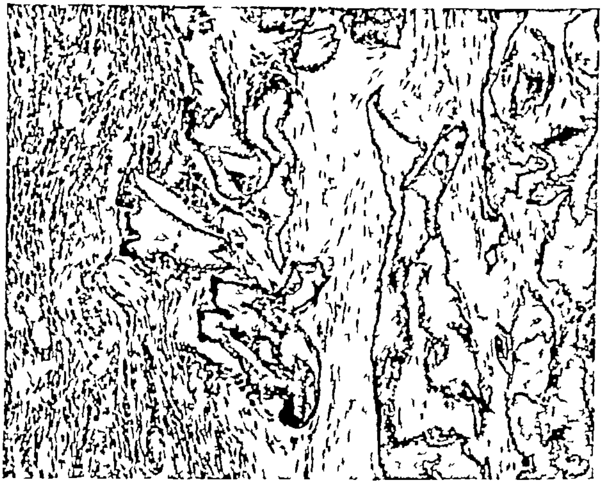

FIG 2 Sections of junction of bladder wall with polyvinyl sponge Cellular collagen permeates deep layers of implant H & E, ×87

omentum which separated easily at this point The luminal surface revealed the polyvinyl sponge partially extruded in all cases with attachment at only a portion of its circumference The sponge appeared brittle, contracted and corrugated (fig 1, *B*)

Microscopic sections identified the polyvinyl sponge as coarse spicules with irregular, sharply angulated interstices The spicules consisted of a pink matrix containing variable-sized, ovoid structures resembling cellules The basal surfaces of the sponge were incorporated into the connective tissue which formed a scar at the site of resection Cellular collagen permeated the interstices of the deeper portions of the implant (fig 2) Near the luminal surface the interstices were filled with fibrinopurulent exudate Some of the spicules showed a rim of basophilic material resembling calcium, others showed bacterial masses and cellular debris None of the implants were completely epithelialized At least one implant appeared to have undergone physical alteration The matrix was fragmented and deeply basophilic Others displayed a lesser degree of basophilia within the matrix Multinuclear giant cells were noted in several specimens, situated on the surfaces of the spicules

A variable degree of acute inflammatory reaction occurred in and adjacent to the deep surfaces of the implants as shown by areas of fibrinopurulent exudate Reactions of the bladder adjacent to the polyvinyl sponge included foreign body granulomas about sutures, squamous metaplasia, epithelial papillations, cystitis, osseous metaplasia and focal peritonitis

Urine culture resulted in no growth in one animal In another, a growth of Gamma streptococcus and coliform bacillus was present A moderate growth of gram-positive, pleomorphic rods was noted in the remaining two animals

DISCUSSION

Wound sepsis at the graft site, however slight, undoubtedly is a deterrent to firm fibrous union Previous investigators (Schofield, Hallenbeck, Grindlay and

Baldes) have described such findings in one case Calcium salt deposition is common to foreign bodies in the urinary tract Whether polyvinyl sponge has an unusual affinity for such deposition is not clear from this experiment Calcium salts have been recognized at 3 months in polyvinyl sponge reinforcement of vascular grafts (Mortensen, Edwards, Grindlay and Kirklin)

The bladder being a hollow, muscular organ subject to periodic expansion and contraction may account, in part, for the limitation in firm union between bladder and polyvinyl sponge Excessive compression of the sponge during heat molding can result in inadequate infiltration of collagen and fibroblasts Preliminary studies with a more porous sponge, however, resulted in peritonitis from urinary leakage

The results indicate polyvinyl sponge to be unsuitable for replacement of bladder defects under the conditions of this experiment Failure of firm union between bladder and polyvinyl sponge resulted from inadequate collagen infiltration of the interstices

In all the animals the material appeared to act as a foreign body Tissue reaction was obvious microscopically while grossly the implants were found to be partially extruded into the bladder lumen with healing beneath

SUMMARY

Experiments conducted with six dogs utilized polyvinyl sponge for replacement of surgically created bladder defects

The sponge failed to incorporate with the normal bladder tissue by firm fibrous union Lack of adequate collagen infiltration was evident microscopically Grossly the implants were partially extruded into the bladder lumina

Wound sepsis, calcium salt deposition, excessive compression of the polyvinyl sponge and rhythmical mobility of the site of implantation are the factors offered to explain the unfavorable results

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RECONSTRUCTION OF THE BLADDER WITH A SEROMUSCULAR GRAFT

EDWARD W CAMPBELL

From the Department of Urology, Hahnemann Medical College and Hospital, Abington Memorial Hospital, Philadelphia, Pa

The concept of bladder substitution or reconstruction is not new The successful construction of a bladder to meet all the requirements of an ideal substitute is, however, a recent attainment The ideals required, and which have been attained are 1) ability to void through the urethra, 2) a reservoir capable of distension and contraction, 3) urinary control, 4) an alarm mechanism to indicate the need to void, 5) ability to obtain sterile urine, 6) the absence of mucus, 7) absence of reabsorption of electrolytes

Grotzinger, Shoemaker, Marucci, Ulin and Martin[1] in 1954, published the results of their initial attempts to reconstruct a bladder with a nonsecreting surface using an inverted seromuscular graft from the ileum Shoemaker and Marcucci[2] elaborated these experiments to develop an improved technique of reconstruction They also constructed bladders in control animals using mucosal and submucosal surfaces for an inner lining All the new bladders functioned equally and normally However, the serosal lined bladder was the only one which produced no mucus, could be sterilized and provided no electrolyte absorption Since that time many serosal lined bladders have been reconstructed in animals and a few in the human patient All of these have served to prove the validity of the initial experimental results The first reconstruction in a human subject was performed on February 4, 1954

CASE REPORTS

G M (Abington Memorial Hospital No 6340), a white man age 57 years, was admitted to the hospital on January 27, 1954, complaining of frequent urination and dysuria of 2 years' duration He had been treated continuously during this time and had had considerable antibiotic therapy Two transurethral resections had been performed, a secondary hemorrhage followed the second procedure This was the only history of hematuria When first seen by us, he was voiding 10 times a day, nocturia three times Voiding was accompanied by severe burning, and he was greatly inconvenienced at work

The past history was negative except for a tonsillectomy in 1941, and a demonstrated gastric ulcer in 1934 From that time he had been on a modified ulcer diet which kept him asymptomatic A systemic review was negative except for the urinary tract

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Read at annual meeting of North Central Section of the American Urological Association, Cleveland, Ohio, October 3–5, 1956

[1] Grotzinger, P , Shoemaker, W , Marucci, H , Ulin, A and Martin, W L The use of inverted seromuscular grafts from the ileum for reconstruction of the urinary bladder Ann Surg , 140 834, 1954

[2] Shoemaker, W and Marucci, H The experimental use of seromuscular grafts in bladder reconstruction J Urol 73 314, 1955

Physical examination revealed a well nourished, alert and active man in no acute distress. The recorded admission temperature was 98.6F, pulse 72 and respirations 20. The blood pressure was 108/50. A complete medical examination gave negative findings with the exception of the urinary tract. Abdominal examination was negative. Rectal examination revealed a small, firm prostate gland. The right lateral lobe seemed hard and suggested carcinoma.

Chemical studies revealed hemoglobin of 12.4 mg., leukocytes 11,800, polymorphonuclear cells 69 per cent, lymphocytes 35 per cent, eosinophils 6 per cent. The blood urea nitrogen was 10 mg. per cent, plasma CO_2 20.4 mEq. per liter and the blood sugar 68 mg. per cent. Urinalysis revealed acid urine, specific gravity 1.018, protein negative, pus 3, 5 to 6 red blood cells per high power field and mucus. Bacillus proteus and yeast cells were grown on culture.

Chest x-rays were negative. Intravenous urographic studies revealed a negative upper urinary tract. A deformity was noted in the bladder outline suggestive of a neoplasm. A barium enema study of the colon gave negative findings. No bone changes were noted in the dorsal, lumbar or pelvic bones.

A cystoscopic examination made the day following admission revealed a diffuse area of hyperemia which extended from the vertex of the bladder downward across the posterior wall to the right and around the lower segment of the right lateral and anterior walls of the bladder in a circular manner. The central portion of the inflamed area on the posterior wall was irregularly elevated and presented papillary projections of the mucosa. Tissue resected from this area was reported to show transitional carcinoma. The vesical outlet was irregular due to projections of two nodules. These were resected and found to be benign adenomatous tissue. No tissue was resected from the posterior urethra, for at this point we were thinking of a total cystectomy and prostatectomy. A needle biopsy of the suspicious right lateral lobe of the prostate gland was taken and showed chronic prostatitis with no evidence of carcinoma.

It was our impression from the foregoing studies that the bladder could be removed leaving the trigone and posterior urethra intact. The new procedure was explained to the patient who consented to have it performed. The operation was performed in the following manner on February 4, 1954, after thorough cleansing of the bowel without antibiotics.

Anesthetic agents. Continuous spinal anesthesia of procaine supplemented by pentothal, nitrous oxide and oxygen.

Operative technique.* The abdomen was opened through a generous midline incision. There were no adhesions. No induration of the vesical wall could be identified and there was no apparent lymph node involvement. An elliptical incision was made through the peritoneum around the dome of the bladder. The bladder was completely mobilized to the base of the prostate gland. The bladder was removed leaving a small cuff of tissue about the urethra anteriorly and laterally. Posteriorly the bladder was excised to the edges of the trigone and intramural portions of the ureters. The seminal vesicles were removed with the

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* Technique similar to that illustrated by W. Shoemaker, J. Urol. 74: 458, 1955.

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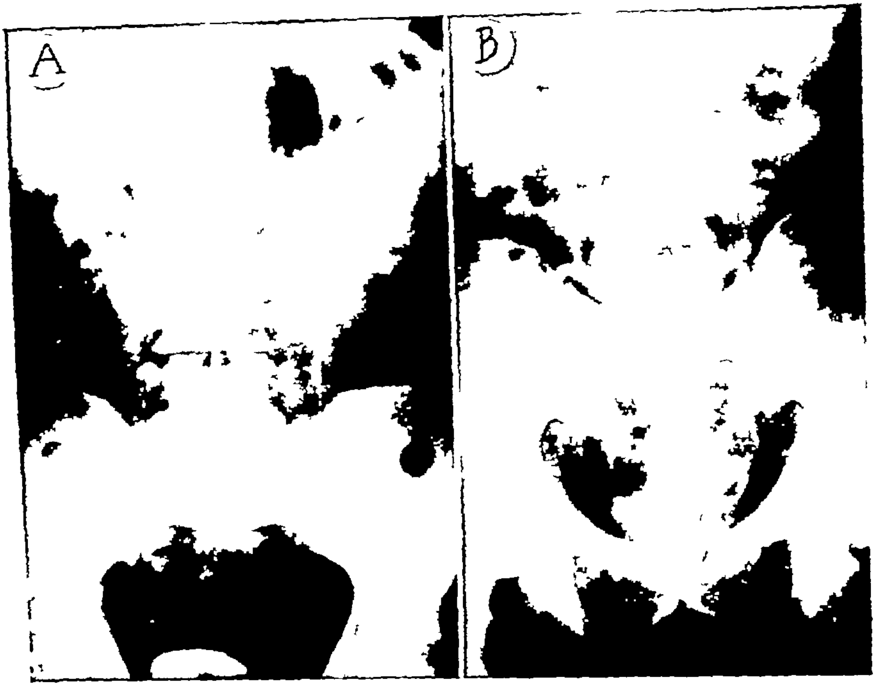

FIG 1 A preoperative intravenous urogram shows normal upper urinary tract and cystographic defect due to tumor B postoperative cystogram reveals reflux on left side Bladder shadow is slightly irregular with suggestion of diverticulum on right side This was site of sinus

suprapubic drainage in varying amounts for 4 weeks when the fistula finally closed and the patient was discharged from the hospital On the tenth postoperative day the wound edges opened down to the fascia and required resuturing which was done with wire sutures

Following discharge from the hospital the sinus reopened and drained intermittently for 3 months when it permanently closed A persistent Proteus infection has been a problem One year following surgery concretions formed which required cystoscopic removal When the patient was last seen on September 19, 1956 the urine was clear a few mucus shreds were present but only a rare pus cell The bladder capacity ranges from 4 to 6 ounces By regulating fluid intake the patient can work without inconvenience and arises two times at night to void His general health is excellent

Chemistry studies made during and following hospitalization were entirely within normal limits The serum CO levels have ranged from 20.4 to 25.7 mEq per liter The blood chloride maximum level was 98.1 mEq per liter Potassium and sodium levels have ranged from 4.9 to 5.0 mEq and 139 to 144 mEq per liter respectively

Cystoscopic examinations made postoperatively have shown a somewhat irregular bladder as suggested by the cystogram (fig 1) The bladder mucosa is slightly more yellow than pink Capillaries can be plainly seen on its surface bladder A loose saline pack was placed in the pelvis following complete hemostasis

The terminal ileum was brought through the wound and a segment 35 cm long was isolated with its pedicle by double clamping and section between the clamps The ends of the ileum were anastomosed anterior to the mesentery of the isolated loop with a continuous No 0000 chromic catgut suture reinforced with interrupted silk sutures The mesentery serving the anastomosed ends was closed on both sides with fine catgut down to the vascular pedicle of the isolated loop The wound and intestines were walled off, except the isolated loop which was brought through the wound and turned upward and laid on saline packs The wall of the ileal loop was cut through all layers with scissors 1½ cm from the posterior mesenteric attachment This permitted laying the ileal segment on the abdomen as a sheet of tissue with the mucosal surface exposed The mucous membrane was dissected with the edge of scissors and with gauze Bleeding was controlled by fine ligatures and hot packs applied to the denuded submucosal surface

The prepared graft was turned over and downward presenting the serosal surface for suturing The outer quarter of the ileal graft was turned downward and inward to approximate its free edges These were sewn together with a Carrell type of continuous suture of No 0 chromic catgut The opposite end of the graft was treated in the same manner A broad, elongated sheet of tissue was thus constructed with an inverted V defect at the center of its lower margin The pack was removed from the pelvis and the graft was brought into the pelvis with ease and with ample length of the mesentery for the anastomosis The base of the V was sutured to the interureteric ridge at its midpoint The free edge of the graft was sutured from this point to the interureteric ridge, around the intramural ureter and to the cuff of bladder tissue about the urethral orifice to the midline anteriorly with a continuous suture of No 0 chromic catgut The opposite side was treated in the same manner This completely enclosed the bladder stump A No 18 Foley catheter was inserted through the urethra and the bag inflated The remaining free edges of the graft were approximated with a continuous suture to complete the reconstruction A small de Pezzer catheter was inserted through a stab wound in the anterior wall of the new bladder The pelvic peritoneum was sutured loosely about the vascular pedicle The abdominal wall was closed with interrupted tension sutures of silk and chromic catgut for the fascia Two Penrose drains were inserted, one to each side of the bladder

A pathological report described diffuse inflammatory changes involving the fundus of the bladder There were two indurated areas which were ulcerated from the resection of tissue for biopsy The pathological diagnosis was carcinoma, transitional cell type, and cystitis cystica

The immediate postoperative course was uneventful Antibiotics were given intravenously until accepted by mouth The maximum postoperative temperature was 100F Peristalsis was present in 48 hours The stomach tube was clamped on the fourth postoperative day and removed on the fifth day Abdominal distension was never a problem

The suprapubic tube was removed on the fifth day following which there was as more reconstructions are performed in the human patient Our first thought for its use was following cystectomy for carcinoma This type of case which I have presented is rare in that the trigone was sufficiently removed from the pathological process to leave it intact It is my opinion that if a cystectomy is indicated in the male patient the entire bladder and prostatic urethra should be removed Following the recent recurrence of carcinoma in the urethral stumps of 2 patients I am seriously considering total urethrectomy in the future In the female patient I have always removed the urethra with the bladder thus precluding this type of reconstruction However in the future urethral reconstruction may be possible with attachment to such an ileal bladder and with control obtained by the use of fascial slings

The transplantation of ureters to the seromuscular bladder is easily accomplished surgically but has not been entirely successful Reconstructed bladders do not have the resilience or the capacity of a normal bladder Therefore reflux and the force of reflux present more of a problem than in simple ureteroneocystostomy

The attachment of a reconstructed bladder to the urethral stump in the male patient offers a problem It is technically difficult to obtain accurate approximation of the serosa to the mucous membrane surface of the urethra without infolding the ileal submucosa with resulting contamination I also doubt the advisability of placing so many sutures through the membranous urethra The use of seromuscular tissue without the submucosa will eliminate this problem by removing the possibility of contamination In this case the graft can be approximated over a catheter with the Vest type of perineal suture

At the present time it seems the foremost indication for the use of a seromuscular bladder is to replace any contracted or irritable bladder an atonic neurogenic bladder or one involved by carcinoma where the trigone and ureteral orifices can be allowed to remain intact Time and more general use alone will tell the advantages of this interesting procedure

The better formed portion of the bladder shows no evidence of suture lines One examining this bladder today would consider it an oddly configured bladder, but I doubt that anyone could guess it had been reconstructed from ileum

DISCUSSION

Some aspects of this report may suggest a discouraging outlook for this operative procedure It must be remembered, however, that our patient was operated upon during the period of early investigation Much has been learned since then and techniques have been improved More recent applications of the procedure have provided firmly constructed bladders with no mucus production and with instrumental infections readily amenable to treatment

The operation is a tedious one and requires meticulous attention to every detail It would be informative at this point to recall the preliminary work of Shoemaker and Marucci[2] in which they demonstrated their inability to completely remove the mucous membrane from the submucosa A suture used to tailor the ileal graft, if passed through the submucosal layer, will provide an opening through which remnants of ileal mucous membrane may grow thereby contaminating the serosal lining of the new bladder Retarded closure of the suprapubic fistula is another means of ingress, as in our report This is now eliminated by limiting drainage to an urethral catheter, and encourages prompt adherence of the outer surface of the graft to the surrounding tissues so that no fistulas have occurred

During the formative period we discussed the use of only serous and muscular layers of the ileum, but thought they were too delicate for successful handling Experimental work with this type of graft is now being undertaken, the advantage of which is not only important from the standpoint of contamination, but facilitates the surgical procedure It is easier to remove the submucosa from the muscularis than the mucosa from the submucosa Suturing is also more easily performed for one does not have to limit the depth of the suture

It is important to get the new organ to function as quickly as possible I am convinced that in any plastic procedure for the formation of tubes or pouches early function and exercise will decide the degree of success Late function leads to contraction and atrophy We have had two experiences which have helped to subtantiate this opinion One was a female patient with complete incontinence, and a contracted bladder due to an Hunner's ulcer A seromuscular graft was placed very successfully in the fundus of the bladder from the surgical standpoint Incontinence prevented early exercise of the graft Tidal drainage would not function because of leakage around the catheter Eventually the graft atrophied and the patient was no better from the surgery

This problem, I believe, will arise with the replacement of neurogenic bladders by ileal grafts These children are incapable of urinary control Such control is a matter of training following operation During the period of training it is essential that bladder exercise be started early and continued until the maximum capacity can be obtained

The indications for this type of procedure will have to be seriously considered

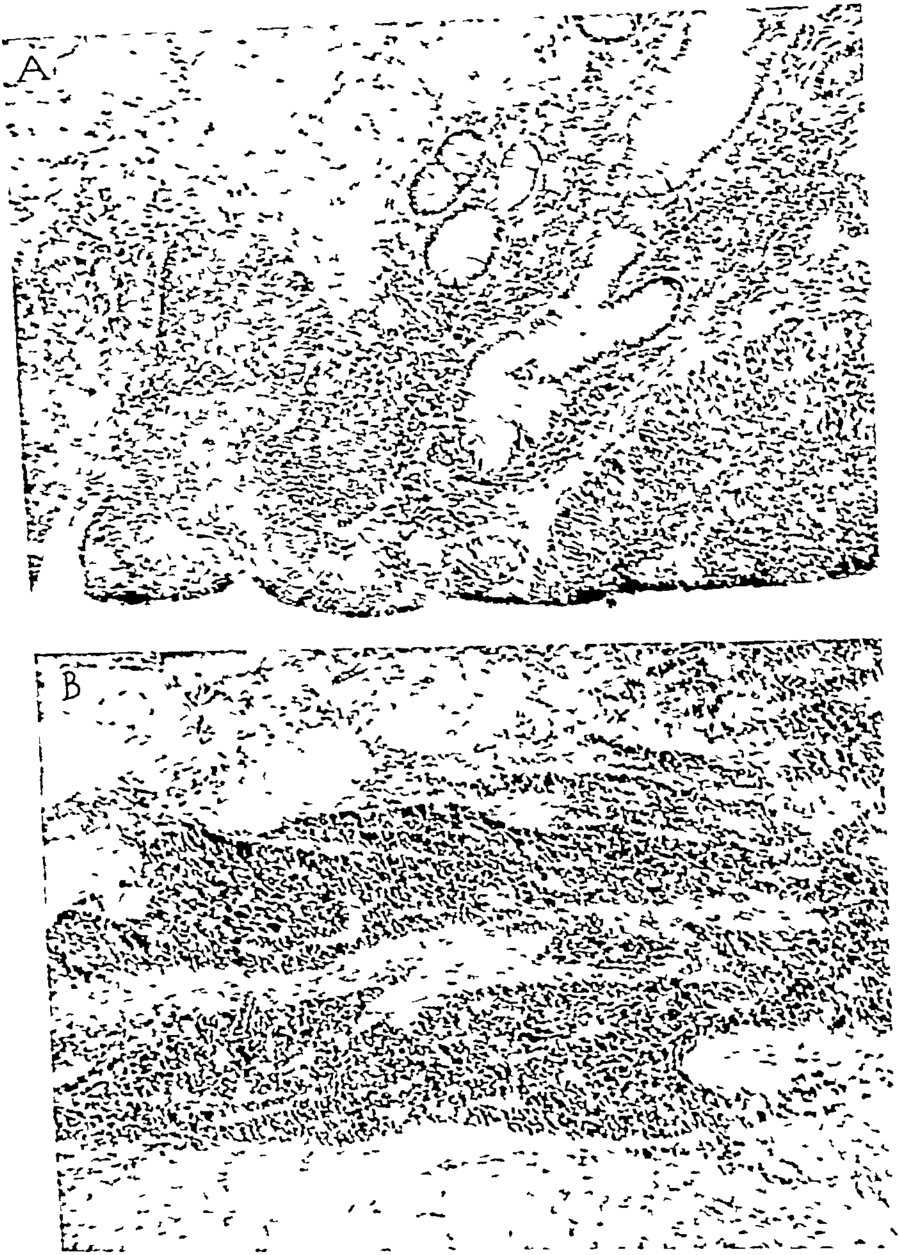

Fig 1 Transitional cell carcinoma *A* similar lesions cover entire mucosal surface Note accompanying colonic type of glands *B* transitional cell carcinoma with deep muscle invasion Section taken from deep within muscularis

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VESICAL EXSTROPHY AND TRANSITIONAL CELL CARCINOMA UNUSUAL LONGEVITY FOLLOWING URETEROSIGMOIDOSTOMY

JUSTIN J CORDONNIER AND HARLAN J SPJUT

From the Department of Surgery, Divisions of Urology and Surgical Pathology, Washington University School of Medicine, St Louis, Mo

The following case report is submitted because of two unusual features, namely, outstanding longevity following ureterosigmoidostomy, and the presence of transitional cell carcinoma in an exstrophy of the bladder

CASE REPORT

The patient was aged 52 At the age of 14, urinary diversion consisting of a bilateral ureterosigmoidostomy was performed by Dr Willard Bartlett, Sr of this city Although the exact nature of the surgical technique employed is not available, it is my understanding that Dr Bartlett used a modification of the Coffey 1 technique The exstrophic bladder was not removed and subsequent efforts to induce the patient to have the bladder removed were unsuccessful In 1939, a hydrocelectomy was performed Nothing in the history suggested urinary sepsis The patient had taken no alkali at any time Fecal and bowel control were excellent Three months prior to this admission, the patient, who was an accurate observer, noted change in the appearance of the exstrophic bladder, and the presence of a watery discharge From that time until he was seen by us there was a rather rapid growth of surface epithelium

On original examination the exstrophic bladder seemed to be covered with multiple papillary lesions with particular involvement about the trigone The blood pressure was 120/80 The nonprotein nitrogen was 16 mEq /L, CO_2 26 6, chlorides 111, sodium 145 1, potassium 3 7 Intravenous pyelograms showed prompt dye excretion bilaterally with essentially normal upper tract configuration There was no evidence of calculus disease Biopsy of papillary lesions revealed transitional cell carcinoma, grade 2

A cystectomy was performed, as wide an area as possible about the bladder being excised Included in the specimen was the peritoneum that covered the posterior surface of the bladder No gross evidence of lymph node or abdominal metastases was seen An excellent repair of the abdominal wall was obtained without too much difficulty, and the wound closed with a small drain at the lower angle of the incision The incision healed promptly, and convalescence was uneventful

Pathology report The bladder measured 9 cm in diameter A cuff of skin surrounded the bladder The exposed surface was covered with extensive papillary and papillomatous gray-white excrescences The skin and bladder edges gradually merged with the papillary components The remnant of the right ureter was identified, its orifice being surrounded by papillomatous tissue Cross-sections of the bladder demonstrated fibrosis and evidence of invasion of the muscularis

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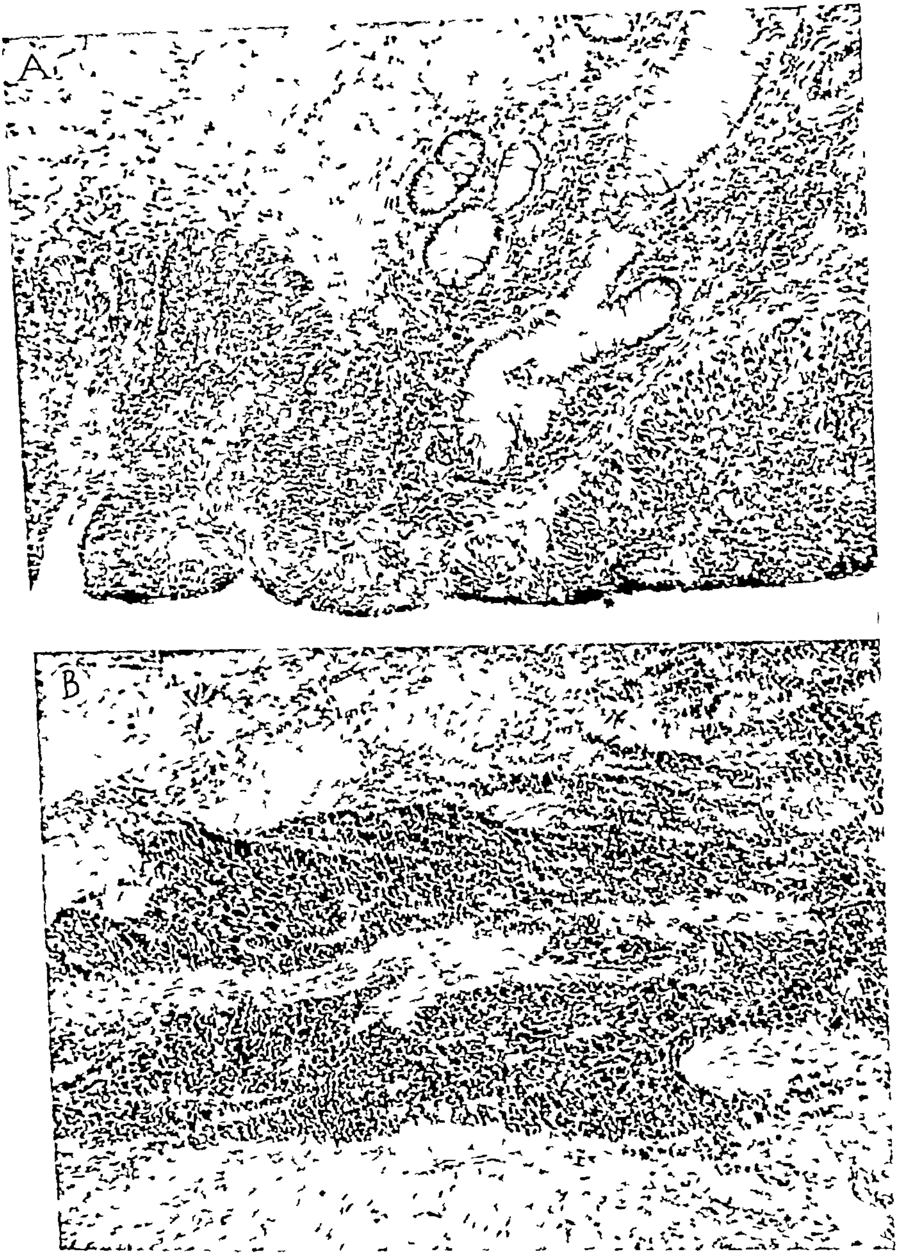

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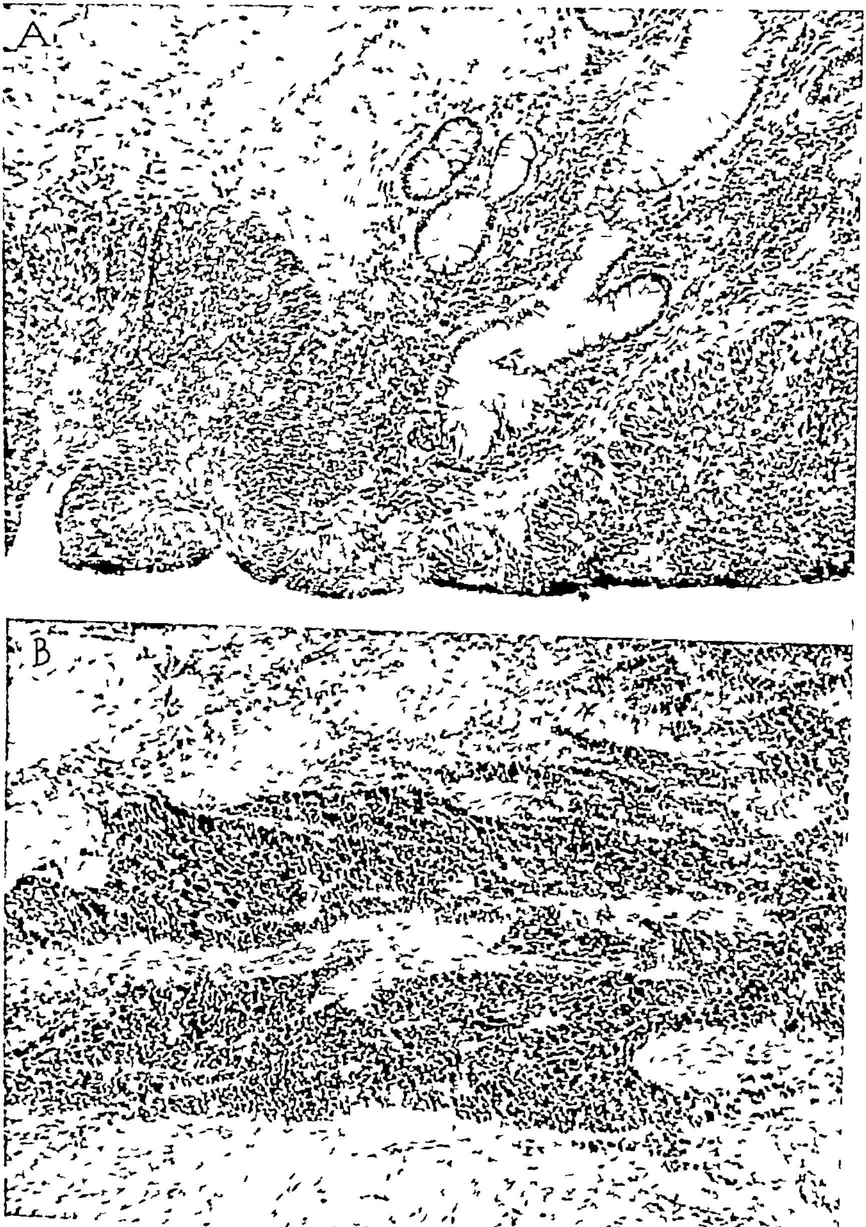

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by carcinoma There was no evidence of extension beyond the confines of the bladder

Study of microscopic sections Eight random sections of the bladder showed a grade 4 transitional cell carcinoma and carcinoma in situ (fig 1, *A*) Much of the carcinoma was superficially ulcerated Invasion through three-fourths of the muscularis was seen in several areas (fig 1, *B*) Intermingled with the neoplasm were foci of squamous metaplasia, leukoplakia, transitional epithelium and numerous groups of colonic type glands The latter did not appear to be malignant Nerve sheath and vascular invasion were not seen

In summary, it was believed that grade 4 invasive transitional cell carcinoma accompanied by carcinoma in situ involved the entire exstrophic bladder epithelium

DISCUSSION

Longevity following ureterosigmoidostomy such as seen here is a very rare phenomenon The last comprehensive review of longevity following uretero-intestinal anastomosis was made by Stevens[1] in which he reported that of 38 patients who had lived 10 or more years, eleven had lived 20 or more years, and two over 30 years The longest recorded survival following ureterosigmoidostomy is 43½ years, a patient of Fowler's However, the case report on this patient stated that he had a staghorn calculus in one kidney and some decreased function in the other It is noteworthy that our patient has essentially normal functioning kidneys and that all electrolyte studies are normal

Of the previously reported 43 cases of carcinoma complicating exstrophy of the urinary bladder, adenocarcinoma has been the predominant histological type No transitional cell carcinomas have been reported, although six of the cases have not been accompanied by histologic detail Transitional cell epithelium is present in the exstrophic bladder at varied ages, as borne out by the reports of Graham,[2] and Goyanna and associates[3] Therefore, it seems incongruous that transitional cell carcinoma should be so rare in the exstrophied bladder However, Von Brunn's crypts and cystitis cystica and glandularis, probable precursors of adenocarcinoma of the bladder, are frequent findings in the exstrophic bladder It is our impression that in all cases of exstrophy of the urinary bladder in which the bladder remains exstrophic until late in life, carcinoma is an almost inevitable finding

SUMMARY

A case of unusual longevity following ureterosigmoidostomy with unusual pathological changes in the exstrophic bladder has been presented

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THE ROENTGENOGRAPHIC DIAGNOSIS OF CYSTITIS EMPHYSEMATOSA

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Cystitis emphysematosa may be defined as an inflammatory condition of the urinary bladder associated with the presence of gas vesicles in the bladder wall

The condition is usually produced by gas-forming bacteria belonging to the colon group and is often associated with diabetes mellitus or hyperglycemia due to intravenous fluid therapy

Diagnosis was first made at autopsy by Hueper[1] in 1926 when these gas cysts were discovered incidentally during postmortem examination In 1932, Ravich and Katzen[2] made this diagnosis at the operating table during cystotomy performed for control of intractable bladder hemorrhage

Cystoscopic diagnosis of this condition was first reported by Burrell[3] who in 1936 described the "small, spherical, transparent, silvery globules having the appearance of air bubbles "

While diagnosis of this condition had thus been made at autopsy, operation, and cystoscopy, no mention of x-ray diagnosis appeared in the literature until Redewell[4] in 1934 suggested the introduction of O_2 into the bladder through a specially devised apparatus requiring collection of the gas under boric acid solution and its injection into the bladder by means of a bivalve syringe such as was used in transfusion therapy He stated that the oxygen cystogram (air was avoided because of the danger of air embolism) in some cases "will clearly depict a swollen bladder wall in which rarified areas can be discovered, which, the author believes, is pathognomonic of extensive gas collection in the wall of the urinary bladder "

Lund, Zingale, and O'Dowd[5] in 1939 described a narrow radiolucent ring about the bladder as a specific diagnostic feature of the disease This was visible in a flat film of the abdomen

Wilhelm[6] also in 1939 reported a case of cystitis emphysematosa in which "a flat x-ray plate showed the bladder wall outlined by gas Excretory pyelography revealed normal function, and outlines of both kidneys, the pelves, and ureters were also normal On the early plates the bladder was filled with gas "

In 1943, Burns[7] reported a case confirming the findings of Lund, Zingale, and

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One may reasonably ask how long these roentgenographic findings persist in these various stages It is probable that the duration of these respective phases varies with each individual case depending on the duration of the infection, the gas producing capacity of the individual infecting organism, the presence and degree of hyperglycemia, the speed with which the infection is brought under control, and finally, the response of the organism to chemotherapeutic or antibiotic therapy Wheeler in his review of the duration in 14 patients in whom the condition was diagnosed antemortem reported the duration to be as follows 3 to 4 days in 3 patients, 5 to 7 days in 1 patient, 10 to 21 days in 4 patients, "disappeared rapidly" in 4 patients, no mention in 2 patients

In this group seven were diabetic and seven were nondiabetic

It is apparent, therefore, that this condition is short-lived and these stages probably blend rather quickly each with the other

The following 2 case reports are presented to illustrate the roentgenographic findings and some of the clinical characteristics of this condition

CASE REPORTS

A 74-year-old married woman was admitted to the hospital because of a 3-day history of frequency of urination, nocturia, and dysuria Eight hours before admission, she noted gross painless hematuria She gave no history of pneumaturia, renal colic, chills, or fever

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Physical examination revealed a thin woman in no acute distress Tempera-

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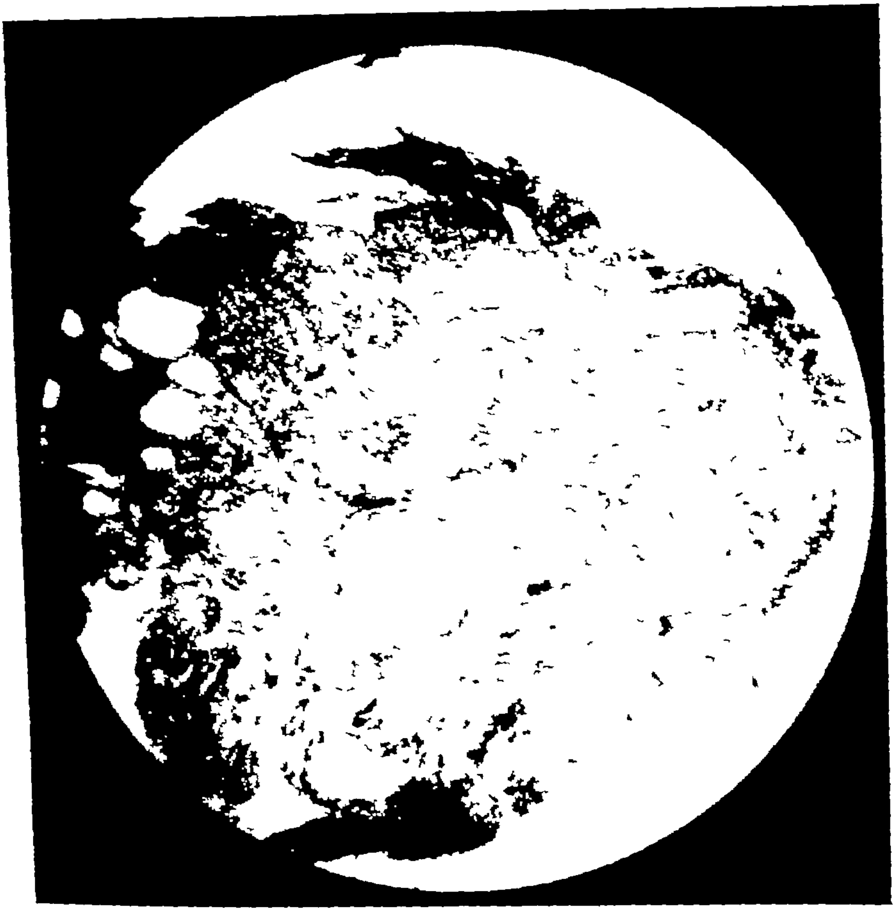

FIG 2 Bladder biopsy Note gas filled blebs in bladder wall with diffuse infiltration of bladder wall by inflammatory cells

A low carbohydrate diet with adequate doses of insulin was ordered along with terramycin The temperature rose to 100 2F on the first hospital day but returned to normal by the third day when hematuria ceased

Another cystoscopy 4 days after the initial examination showed complete disappearance of the gas filled cysts but the hemorrhagic cystitis persisted

A plain urogram taken the same day showed disappearance of the radiolucent ring shadow around the bladder (fig 1 *D*)

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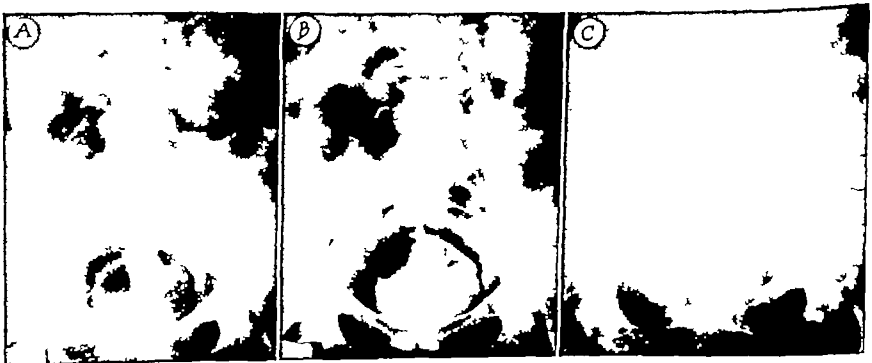
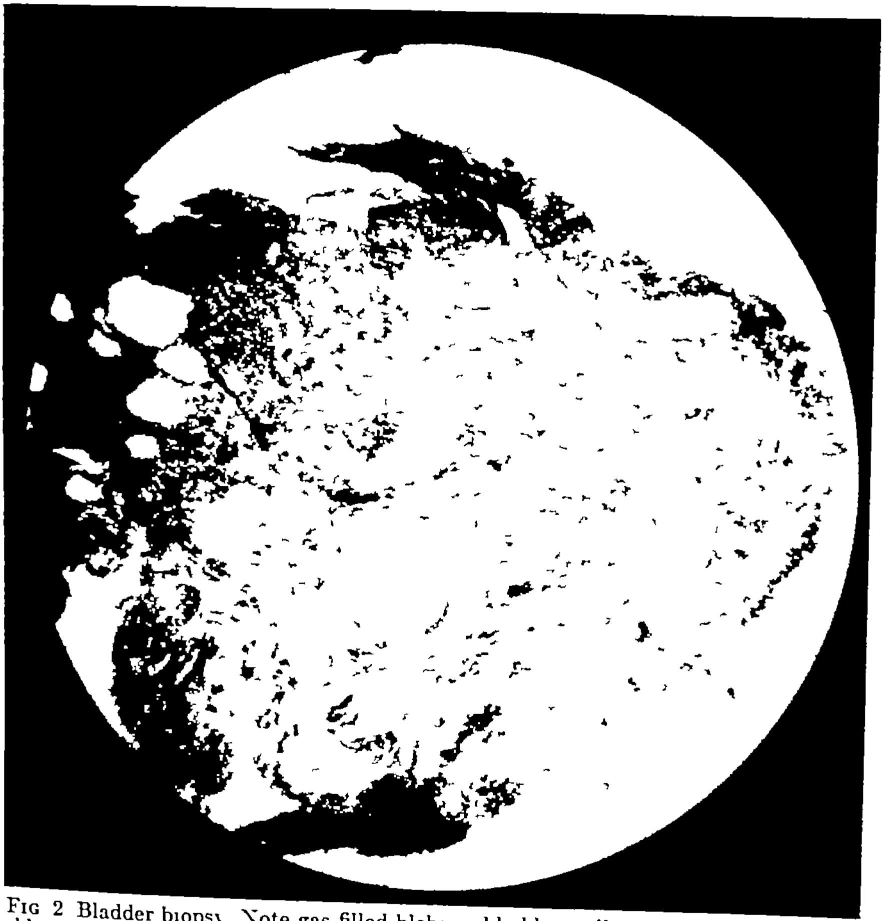


FIG 1 *A*, note characteristic radiolucent ring shadow in bladder region due to cystitis emphysematosa *B*, intravenous pyelogram taken 30 minutes after *A* With increasing distention of bladder by urine, concentric ring shadow changes its position and shape *C*, ring shadow disappeared 4 days after its initial demonstration in *A*



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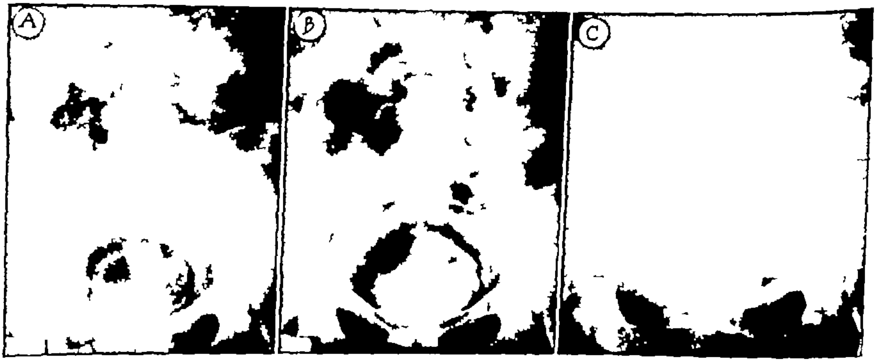

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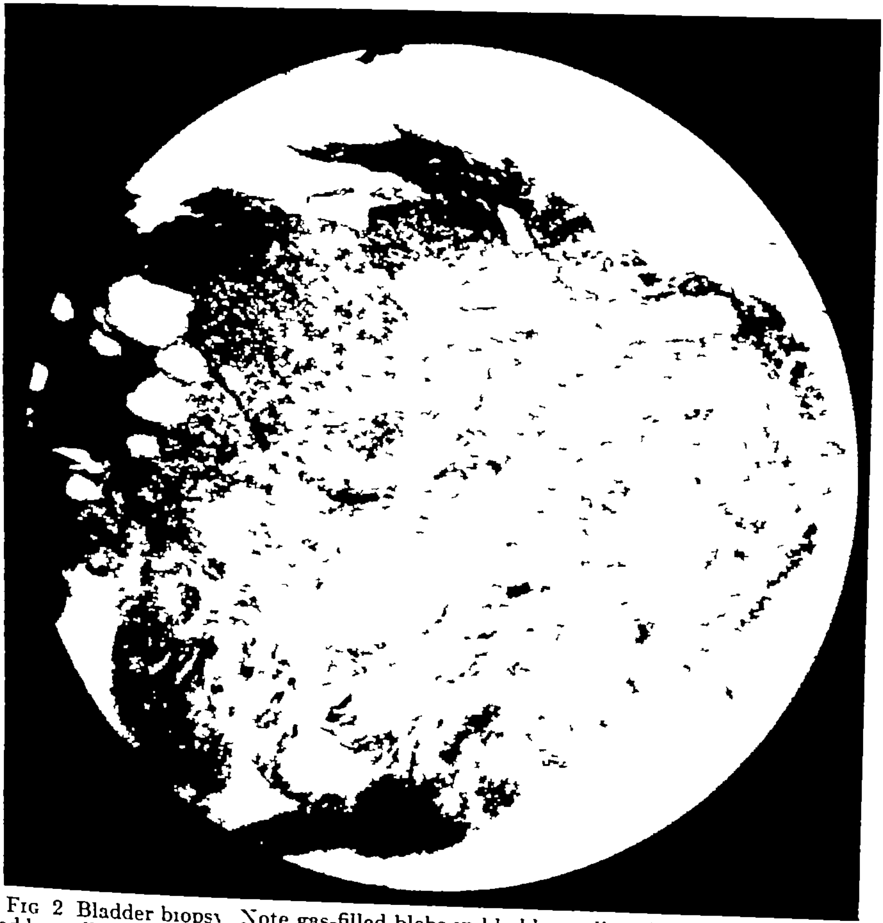

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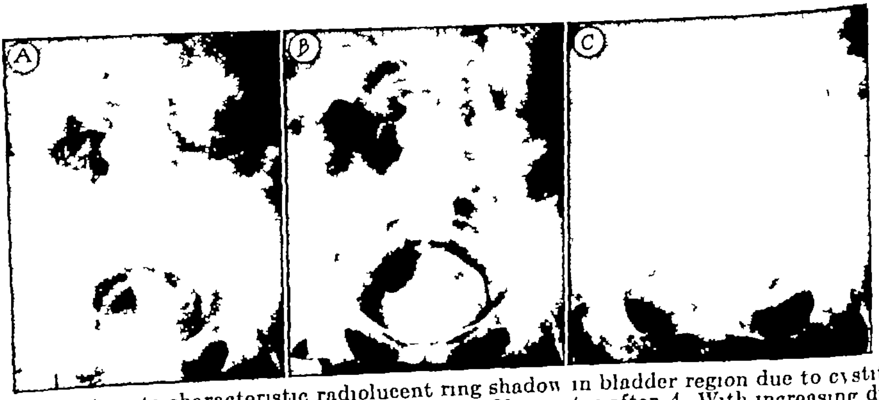


FIG 1 *A*, note characteristic radiolucent ring shadow in bladder region due to cystitis emphysematosa *B*, intravenous pyelogram taken 30 minutes after *A* With increasing distention of bladder by urine, concentric ring shadow changes its position and shape *C*, ring disappeared 4 days after its initial demonstration in *A*

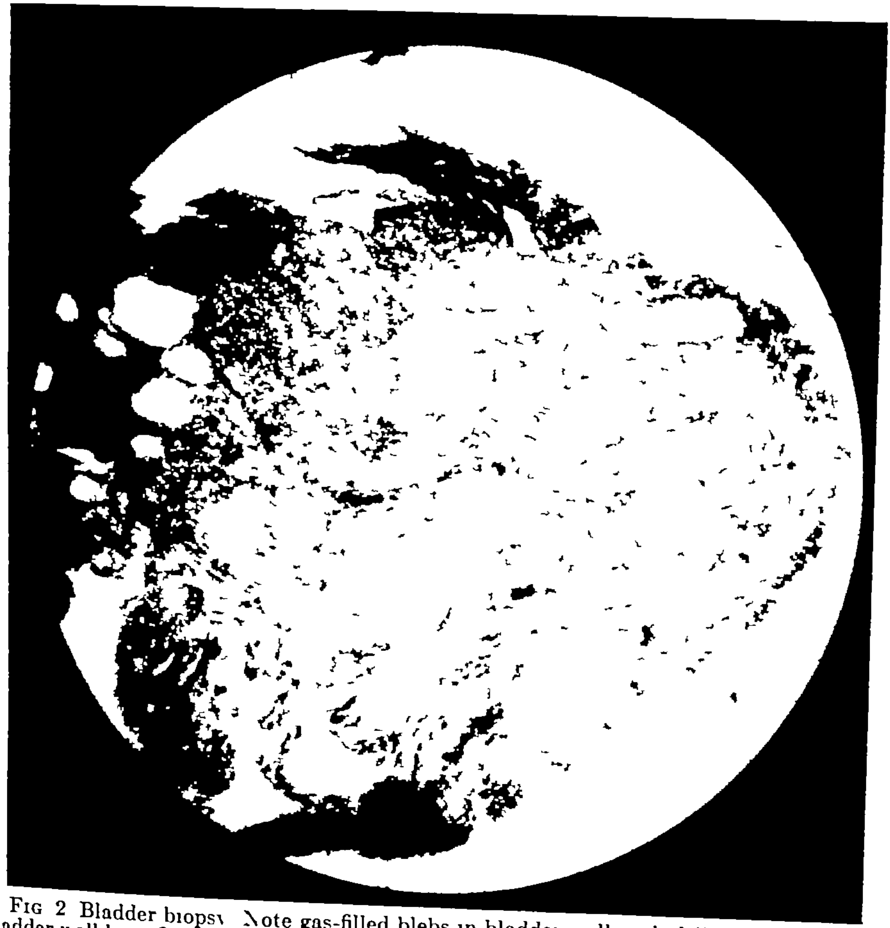


Fig 2 Bladder biopsy Note gas-filled blebs in bladder wall with diffuse infiltration of bladder wall by inflammatory cells

A low carbohydrate diet with adequate doses of insulin was ordered along with terramycin The temperature rose to 100 2F on the first hospital day but returned to normal by the third day when hematuria ceased

Another cystoscopy 4 days after the initial examination showed complete disappearance of the gas filled cysts but the hemorrhagic cystitis persisted

A plain urogram taken the same day showed disappearance of the radiolucent ring shadow around the bladder (fig 1, *D*)

The patient became asymptomatic and was discharged on the tenth hospital day She was taking 58 units of protamine insulin daily before breakfast

Case 2 A 75-year-old white man was seen in consultation because of pneumaturia of 4 days' duration He gave no history of hematuria, renal colic, or chills

His past history was significant in that he had had a suprapubic prostatectomy 20 years previously This was followed by an urethral stricture requiring dilata-

tion every 3 to 6 months In addition he was found to have diabetes mellitus 9 months previous to the present admission This was well controlled by diet without insulin The last urethral dilatation had been accomplished 4 months previously

Physical examination revealed a rather obese man Significant physical findings were blood pressure 179/90, pulse 90, respirations 24, temperature 99F Neither kidney was enlarged or tender No costovertebral angle tenderness could be elicited on either side The suprapubic scar was well healed No suprapubic mass or crepitus was elicited External genitalia were not remarkable Rectal examination revealed a firm, symmetric, surgical prostatic capsule Normal anal sphincter tone was found Extremities were not remarkable Neurological examination was negative

Laboratory studies showed the red blood count to be 3,790,000, white blood

FIG 3 Large collection of intraluminal gas has yielded spontaneous "gas cystogram"

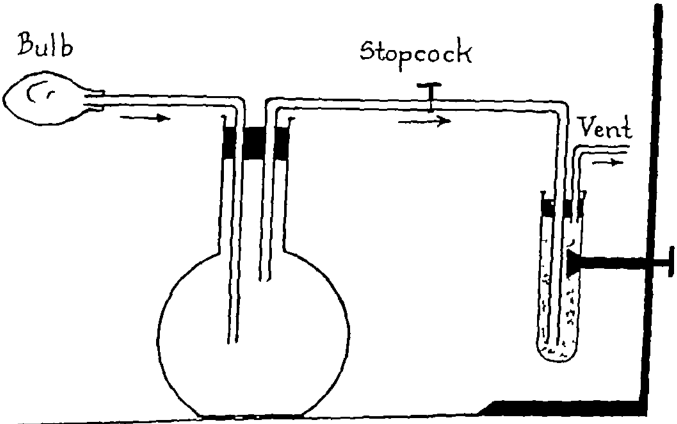


FIG 4 Apparatus designed to demonstrate formation of carbon dioxide from bacteria growth Flask contains medium and bacterial growth Test tube shows $CaCO_3$ precipitate water as gas in flask is forced through apparatus by compression of bulb

count 8 300 hemoglobin 75 per cent The urinalysis showed 1 plus albumin 1 plus glucose and the sediment was loaded with white blood cells The blood nonprotein nitrogen was 54 mg per cent The blood sugar determination was 200 mg per cent

A plain film showed the bladder filled with gas (fig 3) which escaped following introduction of the cystoscope Cystoscopy showed tiny little gas-containing vesicles disseminated throughout the bladder epithelium and generalized inflammation of the bladder wall Urethroscopic examination revealed the presence of a residual nodule of prostatic fibroadenoma in the right side of the prostatic fossa near the verumontanum In addition an area of stricture was seen in the anterior urethra The anaerobic culture of the urine yielded no growth The aerobic culture yielded a growth of B coli which was found to be a gas-producer The gas elaborated on culture of this organism was then collected and tested in the apparatus illustrated in figure 4 This demonstrated the presence of CO_2 in the gas Sensitivity studies showed the organism to be sensitive to terramycin and furadantin

The patient was started on terramycin therapy followed by a course of furandatin He was placed on a low carbohydrate diet and regular insulin The pneumaturia subsided and the patient became asymptomatic Since this episode there has been no further pneumaturia Urethral dilatation has been repeated every 3 or 4 months and his urine is kept sugar-free on diet without insulin

SUMMARY

The roentgenographic features of cystitis emphysematosa are presented along with a brief discussion of some of the clinical and laboratory findings

The characteristics of the x-ray picture appear to vary depending on the stage of the disease and the relative amounts of intramural and intraluminal gas accumulations present at the time the x-ray examinations are carried out

Two case histories are presented with the x-ray findings illustrating marked intramural gas accumulation in case 1 and marked intraluminal gas accumulation in case 2

371 Essex St Lawrence Mass (E J G)

plasm In retrospect, a suspicion of cancer might have led to endoscopic biopsy at a time when radical excision could have been hopefully employed The futility of the many incomplete measures in providing even palliation is all too clear

Case 3 R A , NYH No 700623, a 62-year-old man, had had dilations for symptoms of urethral stricture for nearly five years A diagnosis of urethral carcinoma, made 18 months earlier, led to the following treatments in Europe over the first three months, two local applications of 100 mg of radium for one hour and for one-half hour respectively, telecurietherapy with a 15 gm bomb for a total of 2646 r to the perineum, 6037 r to "superior droit," and 5145 r to "superior gauche " After an interval of three months and during the succeeding two months, additional therapy was given six intraurethral applications of 100 mg radium for one hour each, telecurietherapy with a 15 gm bomb to the urethra for 4030 r total and to the hypogastrium for 520 r total He continued to have pyuria, pain and difficulty in voiding in spite of repeated dilatations Endoscopically the fixed membranous urethra contained slough but a biopsy did not demonstrate carcinoma and a Papanicolaou smear found only suspicious cells Further dilatations and a transurethral prostatectomy provided great improvement for 15 months when hematuria reappeared A hard mass was then found in the perineum but the inguinal nodes were not palpable Transurethral and perineal biopsy both demonstrated a gland-forming carcinoma (raising the possibility of origination in Cowper's gland as well as in the urethral glands proper, but a beginning in the prostate was excluded by history, physical examination, histological examination of the tissue from the transurethral prostatectomy, and the fact that the slough or neoplasm as viewed endoscopically was always distal to the normal appearing verumontanum) The patient refused further therapy The neoplasm was of an unusual histological type and accordingly might have tended to progress differently than the usual epidermoid cancers of this region He had been told originally that he had a "polyp" in the urethra The radiation therapy may have deterred the growth However, the patient had never been asymptomatic since the onset in spite of the treatments outlined—and in less than two years he had more cancer than ever

Case 4 O S , NYH No 277859, a 38-year-old man, was admitted with indications of a stricture in the membranous urethra Trauma and venereal disease were denied but 15 years earlier the patient had had a green urethral discharge for three weeks A mass 3 by 5 cm between the prostatic apex and the perineum was at first considered to be inflammatory Urethrography revealed narrowness and irregularity in this area Symptoms decreased temporarily with drugs, sitz baths, and dilatations, but open surgical exploration within the month demonstrated an epidermoid carcinoma invading the prostatic apex and the triangular ligament (fig 1) The neoplastic mass was very widely excised and an anastomosis between the upper prostate and bulb was attempted (fig 2) This anastomosis failed largely because of the extensive defect Cystostomy, removal of the remaining prostate, and closure of the vesical outlet were accomplished nine days later Left renal calculi appeared within four months and a perineal fistula drained at intervals The perineal fistula and scarring were widely excised and a

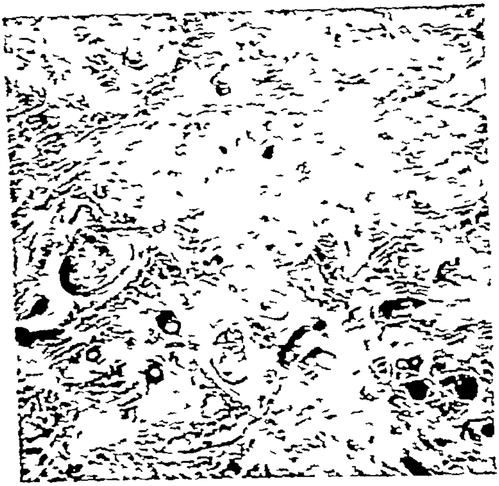
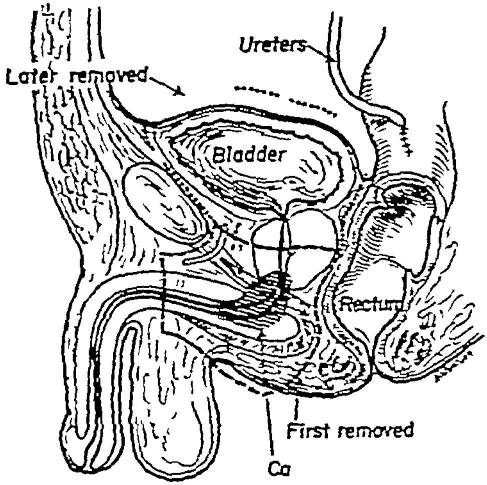


FIG 1 Case 4 Photomicrograph



O.S., N.Y.H. 277859

Nodes not excised
Alive without evidence of cancer, 15 years

FIG 2 Case 4 Diagram of extent of carcinoma and scope of excision.

mobilized gracilis muscle fixed in the dead space The fistula closed for one month only, so this procedure was repeated using the other gracilis muscle with great care to preserve its blood and nerve supply The fistula remained closed for only 48 days The ureters were then transplanted to the bowel by the Coffey 1 technique Two operations were performed later to remove calculi from the left upper urinary tract It was hoped that the cystostomy site would close but it drained periodically so a tube was reinserted However, the bladder remained infected and caused severe symptoms, so simple cystectomy was performed five years after the original excision of the cancer Carcinoma was not found in any

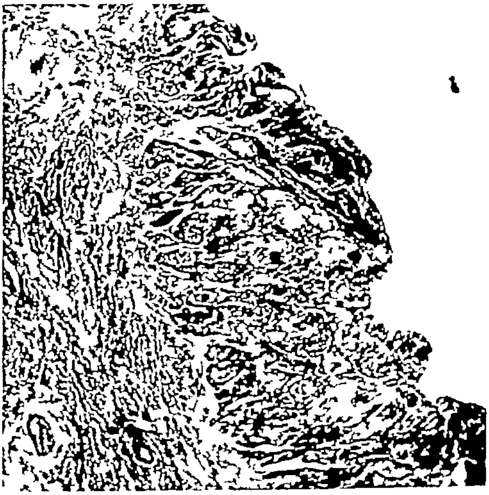
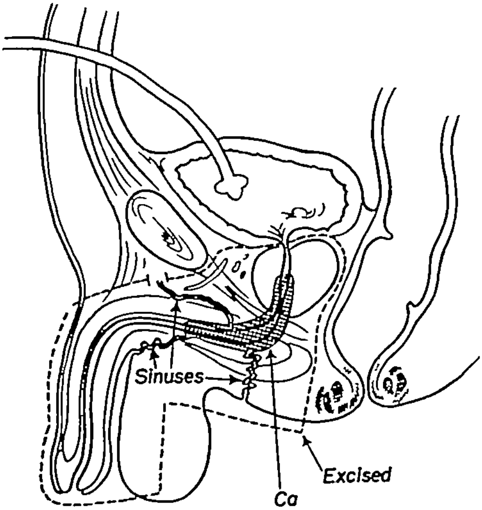


FIG 3 Case 5 Photomicrograph



RB, NYH 279778

Nodes not excised
Died of Pyelonephritis
No Ca at autopsy

FIG 4 Case 5 Diagram of extent of carcinoma and scope of excision

of the numerous specimens removed after the first operation Except for a biopsy of the suprapubic scar (no carcinoma found), no surgery has been employed in the past 10 years Fifteen years, seven months after the first operation there were no clinical evidences of cancer, a nonfunctioning left upper tract on intravenous pyelography, a grade 1 to 2 right hydronephrosis, a small perineal sinus which drained occasionally, and cholelithiasis The inguinal nodes were never clinically suspicious of metastases

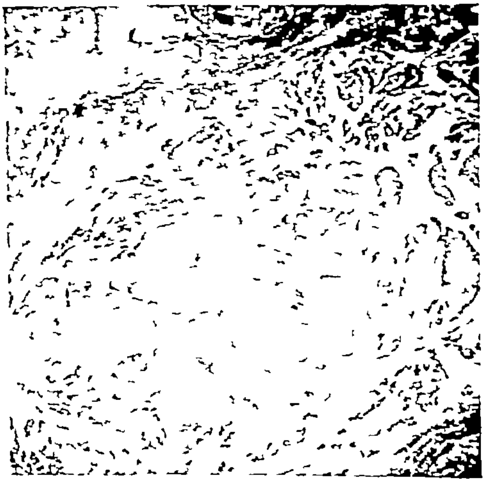


FIG 5 Case 6 Photomicrograph

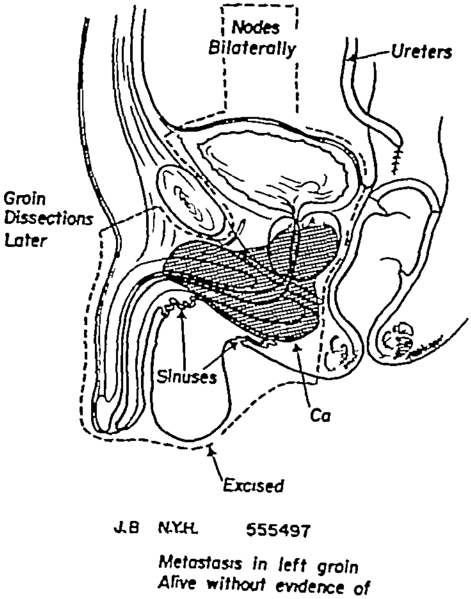


FIG 6 Case 6 Diagram of extent of carcinoma and scope of excision

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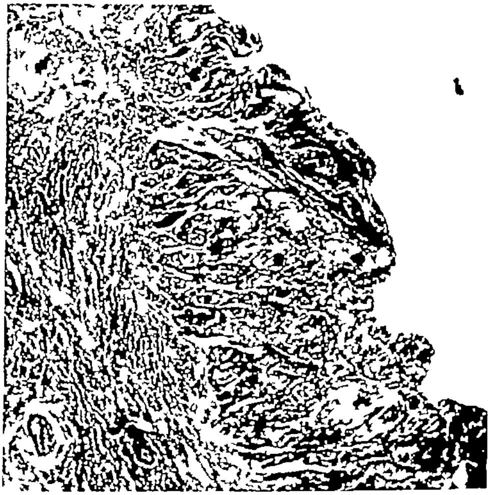

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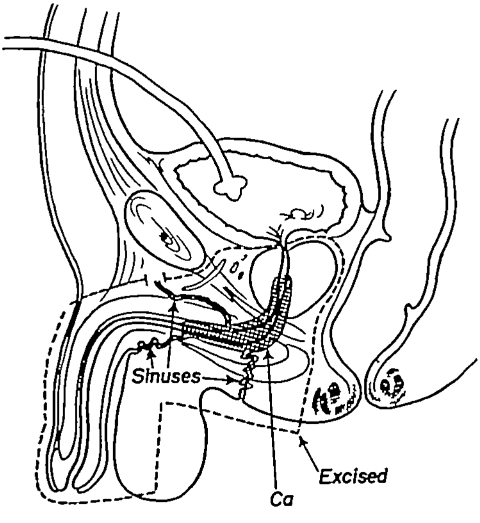

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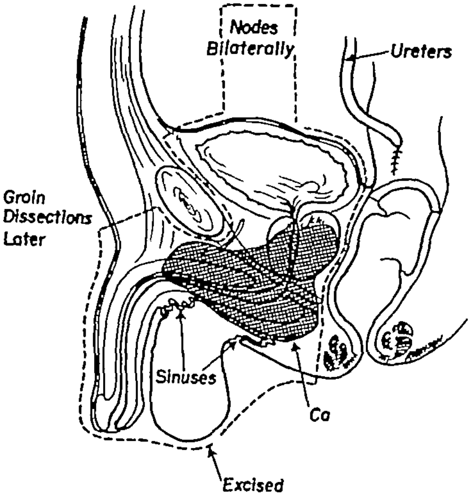

J.B N.Y.H. 555497

Metastasis in left groin
Alive without evidence of
cancer, 6 years

FIG 6 Case 6 Diagram of extent of carcinoma and scope of excision

Case 5 R B , NYH No 279778, a 54-year-old man, was admitted with a cystostomy and draining perineal sinuses of 10 months' duration Following gonorrhea many years earlier he had had urethral dilatations One year previously, obstructed ejaculations were first noted and soon after, a perineal mass Dilations rapidly proved ineffectual so that cystostomy and incision of the perineal mass were performed elsewhere After a biopsy revealed epidermoid carcinoma, 2600 r x-ray was administered to the perineum When transferred from a home for terminal care there were sinuses in the lower left groin, midperineum, and scrotum Induration was palpable from the prostatic apex into the bulb A cystourethrogram demonstrated the sinuses to connect with an irregular deep urethra, bilateral ureteral reflux, vesical calculi, and a left renal stone Biopsy again revealed carcinoma (fig 3) The experience in case 4 caused some changes in our tactics The whole penis, left testis, most of the scrotum and perineum and all the prostate were excised in a block (fig 4) The vesical calculi were removed The epidermoid carcinoma involved the prostatic, membranous, and bulbous urethra but did not invade deeply into the surrounding tissues The vesical neck was mobilized and successfully closed Mobilization of remaining perineal skin and scrotum permitted closure externally with drains The patient was discharged on the forty-second postoperative day, after a smooth convalescence He was readmitted nine days later with chills, fever and uremia Autopsy 58 days after the operation found no carcinoma (including nodes grossly examined and four microscopically examined from the "external" and "internal iliac" regions)

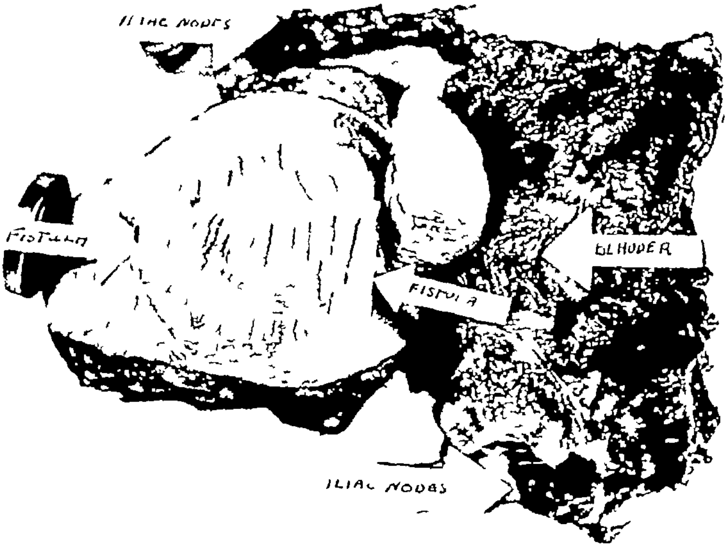

FIG 7 Case 6 Photograph of specimen Inguinal nodes removed later

Bilateral acute pyelonephritis with multiple abscesses, pseudomembranous cystitis, left renal calculi, and bronchopneumonia were the most consequential findings Evidently the cancer had been eradicated with one extensive operation an improvement, but the inadequacies of permanent cystostomy for controlling infection and calculus disease remained as in case 4 The more potent antimicrobial drugs available today might have prevented this early mortality

Case 6 J B, NYH No 555497, a 55-year-old man was admitted with a cystostomy and perineal fistulas He had had gonorrhea and syphilis but had had difficulty voiding for only two months Dilatations and transurethral resection had failed so that cystostomy and incision of a perineal mass were necessary Biopsy revealed epidermoid carcinoma (fig 5) A mass the size of a goose egg extended from the suspensory ligament of the penis back to the prostatic apex Sinuses were present in the perineum and at the penoscrotal juncture The inguinal nodes were not palpable A total emasculation prostatocystectomy with bilateral pelvic node dissection[5] and bilateral ureterointestinal transplants by the Coffey 1 technique were carried out in one operative session (figs 6 and 7) The carcinoma was large measuring 10 cm in one direction, and massively invaded the prostate The pelvic nodes were not found to contain cancer although several in the external iliac group were grossly suspicious He was discharged after 26 days A bilateral groin dissection was performed 90 days after the first operation One node in the left groin measuring 2 5 cm in diameter was replaced with carcinoma (obesity had deterred its earlier detection) The groin

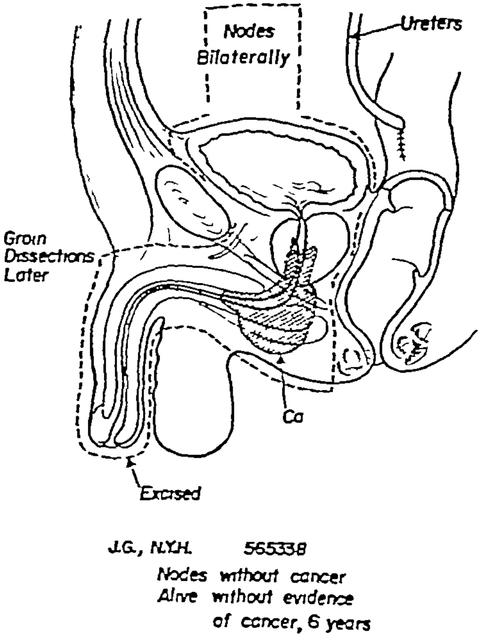

Fig 8 Case 7 Diagram of extent of carcinoma and scope of excision

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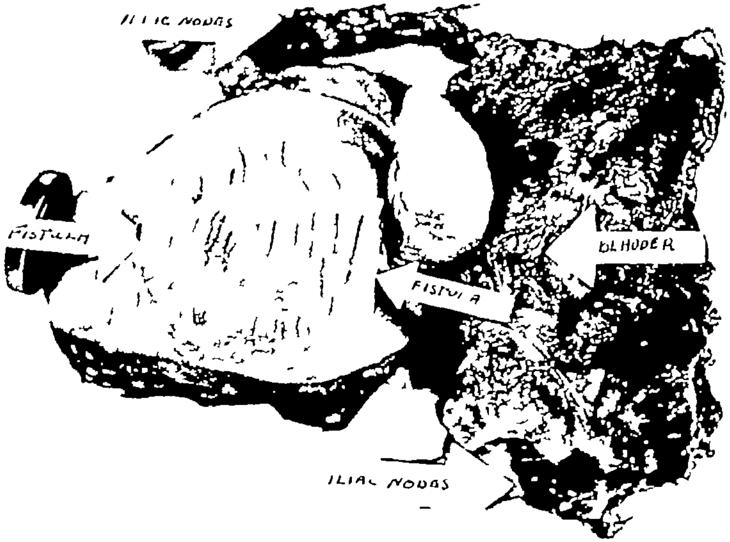

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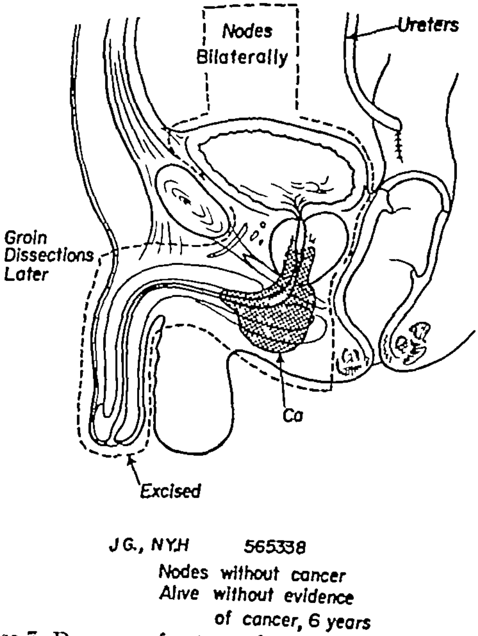

FIG 8 Case 7 Diagram of extent of carcinoma and scope of excision

FIG 9 Case 7 Photomicrograph

wounds partially sloughed and a lymph pocket was drained surgically but eventually all wounds healed Six years after the groin dissection there is no clinical evidence of cancer, but a diffuse lower abdominal hernia, a nonfunctioning left kidney on intravenous pyelography, a minimally dilated right renal pelvis, and a grade 2 dilatation of the lowermost right ureter mar the result He has had no clinical difficulties with the urinary tract, has excellent urinary control, and works regularly In spite of the fact that the circumstances here appeared even more unfavorable than in cases 4 and 5, the more radical approach proved more facile than in case 4 and more successful than in case 5

Case 7 J G, NYH No 565338, a 48-year-old man, was admitted with a carcinoma of the deep urethra previously demonstrated by endoscopic biopsy He had had gonorrhea 25 years earlier and had had increasing difficulties indicative of urethral stricture for three years A 4 by 3 cm perineal mass extended to the prostate The inguinal nodes were palpable but small A total penectomy, radical prostatocystectomy with bilateral pelvic node excision[9] and bilateral ureterointestinal transplants by the Coffey 1 technique were performed at one operative session (figs 8 and 9) The scrotum and testes were not removed The carcinoma measured 7 cm in one direction, was papillary in some areas, and showed a tendency to keratinization in other areas The prostate was grossly invaded but the nodes were not found to contain carcinoma (fig 10) Three weeks later bilateral groin dissection removed glands in which cancer was not found Mild separation of both groin wounds was present but healing and convalescence generally were satisfactory (the highest postoperative temperature was 37 9C on one isolated occasion) Six years after the radical excision there was no clinical

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[9] Paquin, A J Jr and Marshall, V F Technique for radical cystectomy Cancer, 9 585-595, 1956

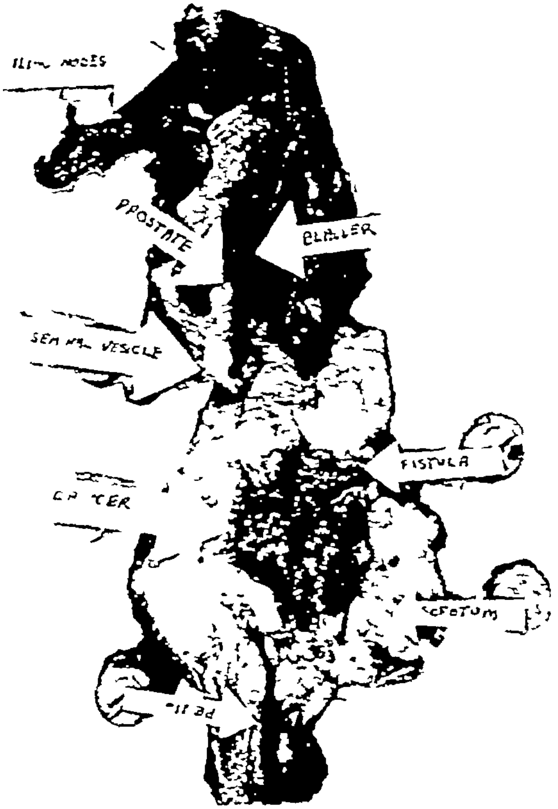


FIG 10 Case 7 Photograph of specimen

evidence of cancer the patient had been working regularly without clinical difficulties with the urinary tract—and the intravenous pyeloureterograms were essentially normal bilaterally ' See figure 11

Case 8 J K NYH No 602513 a 31-year-old man, was admitted complaining of a poor urinary stream of three years' duration An endoscopic examination was said to have shown a urethral tumor 34 months before admission Twenty-eight months prior to admission excision of a mass in the right groin was reported as revealing carcinoma A transurethral resection largely relieved symptoms for a year but the difficulty progressively returned so that for two months catheterization was necessary When first examined by us there was what appeared to be a radiation fibrosis of the lower abdominal skin but the patient gave no history of such treatment (a psychiatric consultant considered the patient to be unreliable) A urethrogram disclosed severe narrowing and irregularity in at least 2 cm of the bulb but no mass was palpable Endoscopic biopsies both of the

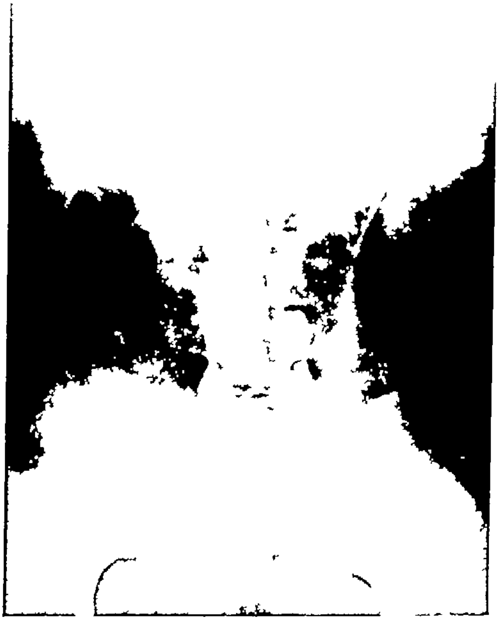


Fig 11 Case 7 Intravenous pyelogram 6 years after bilateral ureterointestinal transplantation by Coffey 1 technique

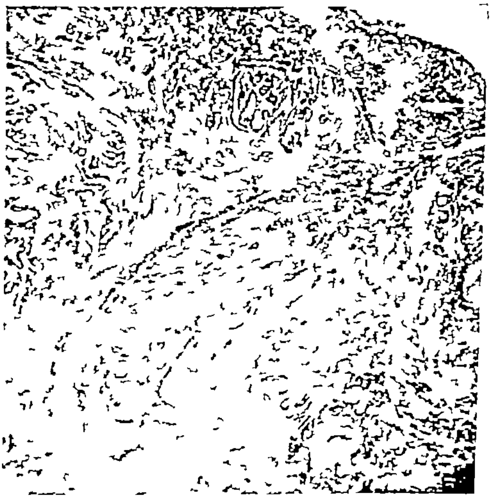
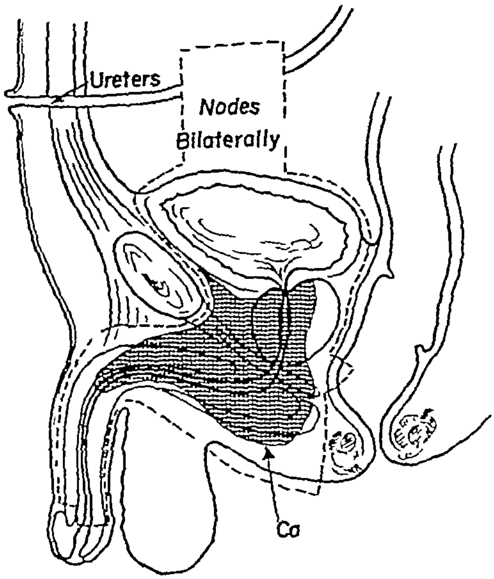


Fig 12 Case 8 Photomicrograph

irregular area and also at the vesical outlet revealed carcinoma (fig 12) All the penis except the glans and skin, the entire urethra with surrounding perineum and perineal skin, the prostate, the bladder, and the pelvic nodes bilaterally were excised during one session (fig 13) The ureters were transplanted to the skin



J.K, NYH 602513

Left external iliac nodes with cancer

A right inguinal node with cancer (History)

Alive, probably without evidence of cancer, 5 years

FIG 13 Case S Diagram of extent of carcinoma and scope of excision

An open injury to the rectum was closed but subsequently it opened and finally closed spontaneously in six weeks Postoperatively, a reactive depression with hysteria developed, and also bilateral thrombophlebitis of the legs, and pulmonary infarction A 4 cm ulcer was found in the urethra, histologically this carcinoma was highly anaplastic with some areas suggesting papillary formations and others, glandular The left external iliac nodes contained cancer but those on the common iliac vessels did not Partly because of the postoperative complications and particularly because the inguinal nodes were not palpable, groin dissections were not performed He was discharged on the fifty-fifth postoperative day The followup has been incomplete but it is known that an abscess about the left ureterostomy was drained 18 months later A letter from him 64 months after the principal operation indicated that although he had had much trouble, including two lithotomies, with the upper urinary tracts, he was working as an automobile salesman From this long letter there is, however, no suggestion of persistent cancer

All these carcinomas treated by radical surgery were fully malignant, invasive, located in the deep urethra and too extensive for local resection The prostate was invaded in each The last five cases constitute our experience in using radical surgery for this disease * The increasing scope of the primary operation with increasing experience did appear to have been an improvement However, the old urological problem of satisfactory permanent urinary diversion remained a major difficulty Cystostomy with vesical neck closure was not satisfactory in two cases (indeed, the one death was directly attributable to this inadequacy) Urinary diversion to the bowel in case 7 provided an unusually satisfactory result Even if cancer eventually reappears, the increased life span and the probable palliation of several years would seem to have made the surgical efforts worthwhile Even the two patients with cancerous nodes remained clinically free of neoplasm after five years Accordingly there is a strong suggestion that nodal excision has been beneficial, and certainly it provided valuable information concerning the nature and extent of the growth Probably these cancers tended to be more localized and more sluggishly metastatic than clinical indications suggested After considering these cases and the reports in the literature, it does seem clear that local extensiveness of a carcinoma of the deep male urethra does not necessarily indicate hopelessness if radical surgery is employed

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* See footnote on p 253

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COMBINED THERAPY FOR PEYRONIE'S DISEASE

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This condition has now become recognized by the entire profession and has been observed at least once by most physicians. Its management, however, still leaves much to be desired whether it be surgical or medical. It is fortunate for the patient that increased interest is being shown in the various methods of treatment offered for from this may come a greater number of cures. The purpose of this paper is to report the results in the management of 186 cases of Peyronie's disease.

The history and pathogenesis have been covered in an earlier article published in 1940. Among the 186 cases observed by the authors, the youngest was 22 and the oldest 84, an average of 53 years. The fifth and sixth decades accounted for 68 per cent of the cases while 87 per cent fell in an age group from 40-69.

A definite history of trauma as the probable etiological factor was given in 61 cases (33 per cent).

As to the location of Peyronie's plaques, in 114 cases the lesions were situated on the dorsal aspect of the shaft of the penis, 13 were lateral and nine were ventrally located. Six cases had more than one area of fibrosis simultaneously. Some 60 cases had the fibrosis near the glans, 41 near or at midportion of the shaft and 29 at the base of the penis. The size varied from the smallest measuring 0.5 by 1.5 cm. to the largest 2 by 8 cm., with the average size 2 by 3 cm. The usual configuration was that of a tennis racquet with the head of the racquet conforming to the most readily palpable portion of the plaque. From this there was a fibrous extension of varying widths and lengths directed proximally comprising the handle of the racquet.

The gross pathology shows a pearl gray, glistening, scar-like tissue measuring 3-5 mm. in thickness with a rather striated appearance, portions of it concentrated into nodular areas. It resembles keloid formation and frequently contains considerable calcium deposition. Cases have been reported that contain cartilage and even bone formation. Microscopically, no evidence of inflammation or round cell infiltration can be found. There are few vessels and many spindle-like cells. Compact bundles of connective tissue comprise the chief architecture. No evidence of malignancy has been found (fig. 1).

Among those cases, as accurately as could be determined, table 2 shows the incidence in frequency of symptoms.

The duration of the presenting symptom on the average was 8.2 months with a maximum of 152 months and a minimum of ½ month. Among the 151 cases in which the duration of symptoms could be determined, 82 cases (54 per cent) reported to the urologist within 6 months and 136 cases (91 per cent) had reported by the end of a year. This is in marked contrast to other more serious dis-

Accepted for publication April 9, 1957.

TABLE 1 *Age incidence*

Decade	Number of Cases	Per cent		
20–29	5	3		
30–39	12	7		
40–49	35	19		87
50–59	76	41	68	
60–69	52	27		
70–79	4	2		
80–89	2	1		
Total	186	100		

FIG 1

cases in which the usual facts are that less than 50 per cent report by the end of the first year

Of the 186 cases observed, 134 received treatment consisting of ultraviolet light, radium plaque either with or without tocopherex, and tocopherex alone Of the 134 cases treated, 90 had only one treatment With reference to application of the radium plaque, 32 cases had two treatments, four had three, five had four, one had five, one had seven, and one case had 11 exposures Of the treatment sites, 34 were retreatments of the original Peyronie's disease while 41 cases had treatments to new sites on the penis A total of 209 treatments have been offered these patients

The total dosage in milligram hours of exposure to the radium plaque varied from 50 to 400 but the latter amount covered more than one location Some patients have had multiple nodules and treatment has been given simultaneously or consecutively depending on the availability of the amount of radium desired The average amount was 120 mg hours for a single treatment

The treatment can be given in the office with a radium plaque held in position by adhesive strips, the scrotum being isolated by a thick lead plate Average time varies between one and two hours The radium plaque itself consists of the desirable number of 12½ mg radium element needles placed parallel and separated from one another by a distance of ¼ inch and screened by 1 mm of lead, the entire construction held together by 1 mm of gum rubber The number of needles per plaque and the number of radium plaques used depend on the size, location and configuration of Peyronie's nodule One should be cautioned to expect some degree of local skin irritation and even a burn (resembling sunburn) with the use of radium

Treatment with mixed tocopherols consisted in oral administration of one 50 mg capsule of tocopherex (Squibb) daily for 30 to 60 days

Complications consisted of an indolent weeping ulcer at site of application of radium in 3 cases All were surgically excised, two with successful outcome, one with failure requiring skin grafting All patients should be followed for a period of at least 2 years before their final status is determined Where desirable, treatment of the same lesion may be safely repeated in 8 months Those cases in which it has been impossible to follow a patient or he has failed to return have been classified as failures

TABLE 2 *Chief complaints*

	Incidence	Per cent
Bend on erection	115	44
Up	73	
Down	10	
Left	17	
Right	16	
Lump on penis	81	31
Pain on erection	53	20
No erection distal to lump	12	5
Total	252	100

TABLE 3 *Results*

Treatment	Cases	Cured	Improved	Unchanged	Lost	Per cent Cured or Improved
Ultraviolet ray	4	1		3		25
Radium plaque	96	39	35	2	20	77
Radium plaque and radon	1			1		0
Radium plaque and tocopherex	31	5	21		5	84
Tocopherex	2			1	1	0
Total	134	45	56	7	26	75

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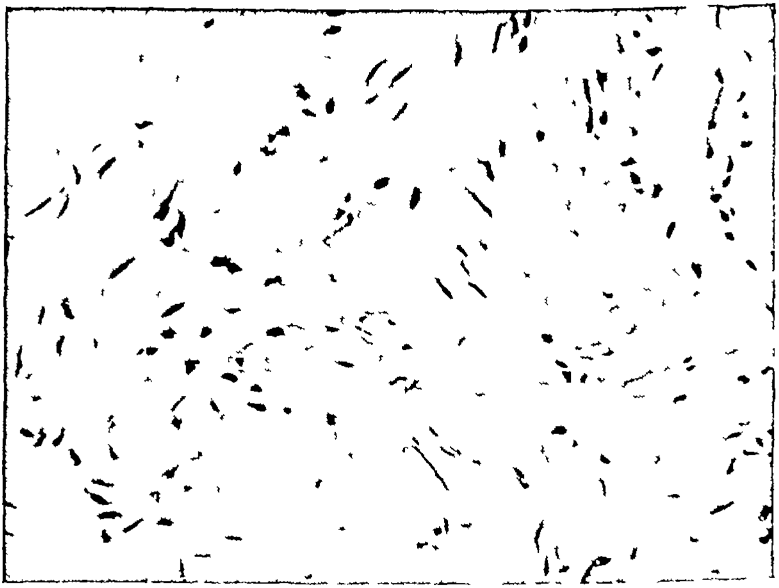

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The total dosage in milligram hours of exposure to the radium plaque varied from 50 to 400 *but the latter amount covered more than one location* Some patients have had multiple nodules and treatment has been given simultaneously

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EMBRYONAL CARCINOMA OF TESTIS IN INFANTS AND CHILDREN: REPORT OF TWO CASES

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Although there are many pitfalls and inadequacies known to be inherent to the use of statistics, the statistical approach remains one of the proved yardsticks in medicine. The physician becomes unusually aware of his dependence on this technique for outlining therapy and estimating prognosis when he turns to the literature only to find that the experience of any single author has been inadequate for the drawing of conclusions of statistical validity. The author was placed in such a position when, within the space of a few months, two children presented with testicular masses which proved to be embryonal carcinoma. It is the purpose of this article to collect from the literature information on this disease as it is seen in children, and thus make available in one place data on which the physician can base his decision.

CASE REPORTS

Case 1. A white child was 2 years of age when first seen. The mother had first noted enlargement of the left scrotum 4 weeks before seeking medical advice. The left scrotum contained a firm, nontranslucent mass measuring 4 by 3 by 2 cm. which replaced the normal structures; a normal cord down to the level of the mass, normal right scrotal contents, no unusual inguinal lymphadenopathy, no palpable para-aortic nodes on abdominal palpation, and no sexual precocity. The chest x-ray, intravenous pyelogram and films taken to rule out metastases revealed only normal findings. Hemogram, urinalysis and a test for urinary gonadotrophins were within normal limits.

Orchiectomy with preliminary high ligation of the cord was performed. Intra-abdominal palpation through the internal inguinal ring revealed no enlargement of the paravertebral nodes (figs. 1 and 2). At the time that this manuscript was submitted the patient had been followed 8 months without evidence of recurrence or metastasis.

Case 2. A Negro child was 6 years of age when first seen. Enlargement of the right scrotum was first noted 2 weeks before admission. The right scrotum contained a firm, nontranslucent mass measuring 8 by 6 by 3 cm.; a cystic mass 2 cm. in diameter was translucent and lay superiorly; a normal cord could be palpated down to the level of the smaller mass; left scrotal contents were normal, no unusual inguinal lymphadenopathy or palpable para-aortic nodes were detected on abdominal examination, and no sexual precocity was evident. X-ray and laboratory findings were normal.

Orchiectomy with high ligation of the cord was performed. Intra-abdominal palpation revealed no evidence of metastatic involvement of the paravertebral nodes. The patient was presented at a tumor conference and, after considerable

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Although other methods have been used to treat Peyronie's disease, the use of the radium plaque, especially supplemented with tocopherex, continues to give us encouraging results Table 3, results, cites the early use of ultraviolet light, yet in spite of its known ineffectiveness, one patient seen 19 years later had apparently been cured of Peyronie's disease Time was probably the explanation for the disappearance of the lesion, as has been witnessed before, yet we had to classify the case as cured

The over-all cure or improved rate in 134 cases treated by all our methods or combination of them was 75 per cent With the radium plaque alone it was 77 per cent and with the combination of radium and tocopherex it was 84 per cent All lost cases were classified as failures

SUMMARY

The use of the radium plaque has proven both safe and effective

Trauma still plays a part in a large per cent of these cases

Smaller, repeated exposure to the radium plaque is the preferred therapy

The combination of the radium plaque with tocopherols has been our most effective method of management with 84 per cent of the cases cured or markedly improved

958 Arcade Bldg , St Louis 1, Mo

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Lowsley, O S and Boyce, W H Further experiences with an operation for cure of Peyronie's disease J Urol , **63** 888–899, 1950

Scardino, P L and Scott, W W Use of tocopherols in treatment of Peyronie's disease Ann N Y Acad Sci , **52** 390–396, 1949

man and Moore[2] found that 19 per cent of their post-war United States Army series were embryonal carcinomas, so that in civilian adults an incidence of less than 0 5 per cent can be estimated Comparable figures for children are not available However, some conception of the statistical probability of the disease can be obtained by appreciating that the incidence of all types of cancer, even in a weighted group like hospitalized children, has been reported as low as 0 26 per cent,[3] and that tumors of the genitalia comprise less than 1 0 per cent of the malignancies of childhood[4] Melicow[5] reports seeing only one instance of embryonal carcinoma in a child during 25 years at the Squier Urological Clinic Additional evidence of the infrequency of this condition is furnished by the literature of the past 45 years These reports yield a total of 28 case reports* from fifteen different sources,[6-20] the largest series (seven) being that of Gross[15]

PATHOLOGY

Until the post-war years, germinal tumors of the testis were usually classified as embryonal carcinoma or adult teratoma[24] No attempt will be made to either reiterate or summarize the several excellent works on the classification of testicular tumors which have appeared by Friedman and Moore,[2] Dixon and Moore[25, 27] and Melicow[5] However, it must be made clear that, particularly in the older literature, authors discussing results of therapy have often not been discussing comparable tumors Histologically there are four types of germinal tumors (seminoma, embryonal carcinoma, teratoma and choriocarcinoma)[25] which may appear in any combination and which have differences in their clinical behavior[25]

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* Magner, Campbell and Wiglesworth[21] have shown that the cases of embryonal carcinoma reported by Meltzer and Bloom[22] and Rosenblum and Robbins[23] are actually clear cell adenocarcinoma, which they show to be a separate clinical and pathological entity Therefore, these 2 cases have been excluded from the discussion

[2] Friedman, N B and Moore, R A Mil Surg, 99 573 1946

[3] Jaureguy M A Arch Pediat Uruguay, 24 316, 1953

[4] Handy, V H and Goldberg, I D N Y State J Med, 56 258, 1956

[5] Melicow, M M J Urol 73 547, 1955

[6] Kutzmann, A A and Gibson T E Ann Surg, 78 761, 1923

[7] Mouchet, M and Derocque, A Bull Soc Anat Paris, 94 484, 1924

[8] Sakaguchi, J Dtsch Ztschr f chir, 125 294, 1913

[9] Shane, J H J Urol, 42 236, 1939

[10] Nakagawa Y Okayama Igakkai Zasshi, 53 160, 1941

[11] Matassarin, F W J Urol, 65 693, 1944

[12] Williams, I G Brit J Radiol, 19 182, 1946

[13] Kretschmer H L Am J Surg, 76 99, 1948

[14] Rusche, C J Pediat 40 192, 1952

[15] Gross, R E Surgery of Infancy and Childhood Philadelphia W B Saunders Co, 1953

[16] De la Peña, A Acta Pédiatr Esp, 62 353, 1954

[17] Frguder, R and Aker O N Deniz Tip Bül 1 30, 1955

[18] Doyle, J B Brit J Urol, 27 287, 1955

[19] Amato, M, De Angelis P and Di Gruttola, G Pediatria, Nap, 64 302, 1956

[20] Sharma, G C and Samuel, K C J Ind M Ass 27 57, 1956

[21] Magner, D Campbell, J S and Wiglesworth, F W Cancer 9 165, 1956

[22] Meltzer, A and Bloom B New Eng J Med, 237 513, 1947

[23] Rosenblum, A and Robbins, M A J Pediat 33 627, 1948

[24] Ferguson, R S Am J Roent 31 356, 1934

[25] Dixon, F J and Moore R A Tumors of Male Sex Organs Washington, D C Armed Forces Institute of Pathology, 1952

[26] Friedman, M in Portmann U V Clinical Therapeutic Radiology New York Thomas Nelson and Sons, 1950

[27] Dixon, F J and Moore, R A Cancer, 6 427, 1953

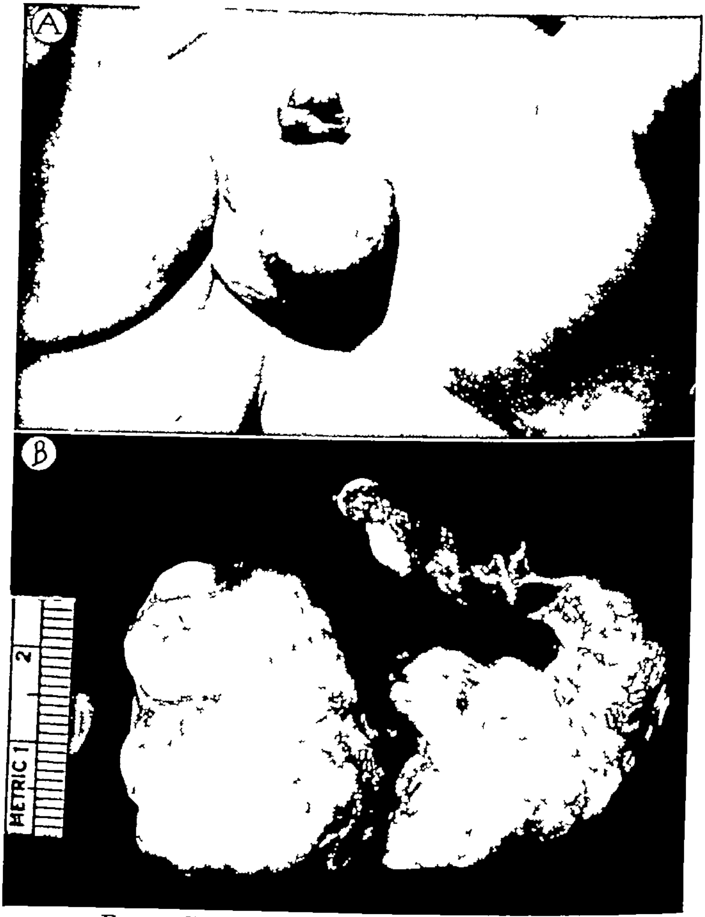

FIG 1 Case 1 *A*, genitalia *B*, gross specimen

discussion, a retroperitoneal node dissection was recommended The dissection was accomplished to the level of, and included the right renal pedicle The nodes surrounding the right common iliac, and the origins of the right external and internal iliac arteries were removed along with the right spermatic vessels Multiple sections of the nodes showed no involvement by tumor (figs 3 and 4)

Three months following surgery the patient was readmitted because of para umbilical pain of one week's duration A firm mass the size of a hen's egg was noted on deep palpation in the epigastrium The intravenous pyelogram showed lateral deviation of both upper ureters, and x-rays revealed a metastatic lesion in the body of the third lumbar vertebra, and another in the greater trochanter of the left femur The urinary gonadotrophins were not elevated At the time of writing, the patient is showing little response to palliative irradiation

INCIDENCE

The incidence of testicular tumors in the adult civilian population has been estimated by Gilbert and Hamilton[1] to be 2 per cent of all malignancies Fried-

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[1] Gilbert, J B and Hamilton J B Surg Gynec & Obst 71 731 1940

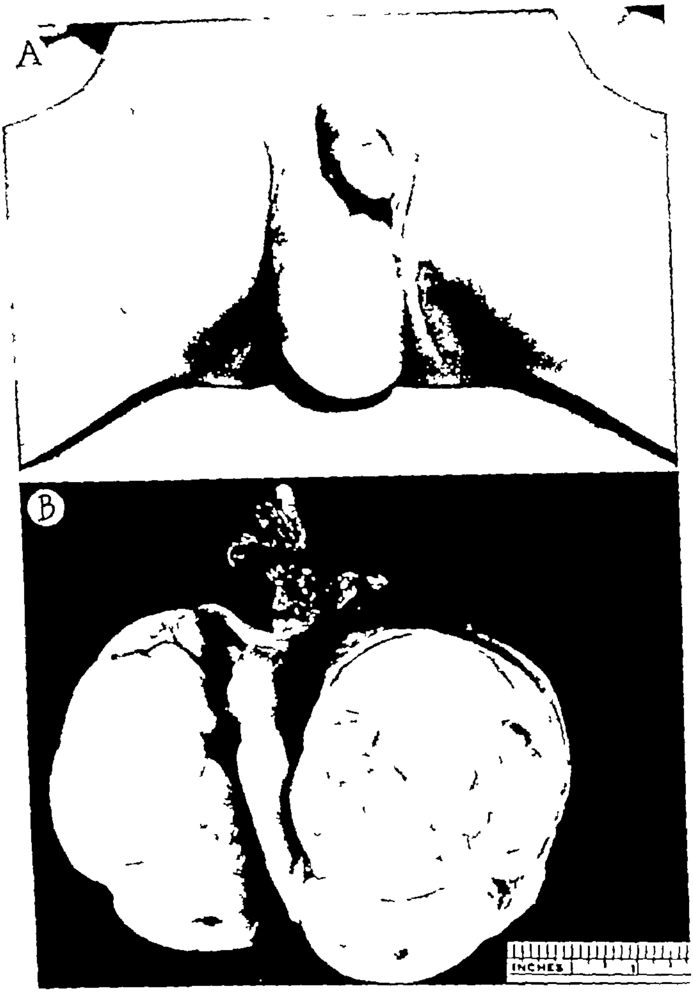

FIG 3 Case 2 *A*, genitalia *B* gross specimen

on the test for urinary gonadotrophins, finding it to be present in significant amounts in 29 per cent of preoperative urines, and noting that patients with elevated assays had an 85 per cent two-year mortality rate as opposed to a 50 per cent rate for those with normal studies The significance of the presence of metastases is revealed by their finding a 92 per cent two-year mortality rate compared to a 46 per cent rate in those with no metastases at the time of operation

COMMENTS ON THE SURVEY

Table 1 shows the age distribution of the patients at the time of diagnosis It is of interest that more than two-thirds are younger than three years

No cryptorchid testes were present in the cases reviewed, although Culp[31] and

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[31] Culp D A J Urol , 70 282, 1953

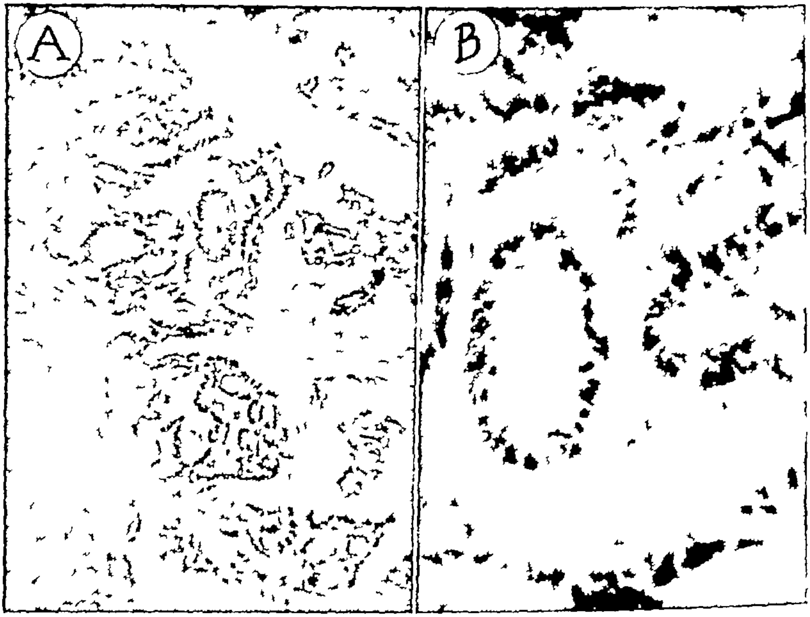

Fig. 2. Case 1. Photomicrographs. *A*, low power. *B*, high power.

Within the limitations imposed by the multiple sources of histologic interpretation, it is highly probable that all considered here are Dixon and Moore's class 2,[25] or trophocarcinoma as defined by Friedman.[26]

INVESTIGATION

Diagnosis is based on a consideration of the physical, radiographic and laboratory findings. A very satisfactory outline is presented by Dixon and Moore.[25] It is worthwhile to note that no mention of pain was made in any case where the disease was confined to the testis. Also, the frequently overlooked feeling of heaviness or a dragging sensation in the testis is not referred to in the literature on children. The laterality of the involved testis is generally regarded as of no consequence, and both sides are involved almost equally.[14 18] Gross[15] emphasizes the importance of searching for metastases in the pelvis and para-aortic region. Metastases do not appear in the inguinal nodes until the scrotum has been invaded. Dissemination occurs through both blood and lymphatic channels, but there appears to be a definite, though indeterminate, period before the tumor is spread via the bloodstream.[28] Higgins and Arber[30] have discussed the lymphatic pathways in minute detail. A point worth emphasizing is that there is frequently early dissemination from the region of the renal pedicle to the opposite side and to the mediastinal and cervical chains. When involvement of the pelvic nodes occurs, it is in a retrograde manner.

Although Higgins and Arber[30] have stated that bioassay in embryonal carcinoma is of limited value, Dixon and Moore[27] have placed considerable emphasis lymph nodes were present It is also noted that documented survival of more than three years occurred in only six instances Although there is not sufficient material to be statistically significant, it is interesting to compare these findings in children with those of Dixon and Moore in adults[27] In their series of embryonal carcinoma the death rate per 100 survivors fell from 40 4 and 30 7 in the first two years to 9 8 in the third year, 2 0 in the fourth and 2 7 in the fifth A comparison may be valid, and is certainly suggestive, as the fall in children is similarly dramatic

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[28] Phillips, R. F. and Dargeon, H. W.: J. Pediat., **44**: 448, 1954.

[29] Lewis, L. G.: J. Internat. Coll. Surg., **26**: 49 (part 1), 1956.

[30] Higgins, C. C. and Arber, F. W.: Canad. Med. Ass. J., **69**: 124, 1953.

Chorionic gonadotrophins were obtained in only four instances All of these proved to be normal When the second patient showed metastases, the test remained normal

TREATMENT

Most of the common methods of therapy were employed in this series, both individually and in combination The situation is comparable to that in music where there is one main theme on which there are many variations The literature on the adult disease indicates that orchiectomy with preliminary high ligation of the cord is considered fundamental to all generally accepted approaches This is usually followed by retroperitoneal node dissection and/or prophylactic roentgen therapy[5, 27, 33, 34] Dean[35] believes that extensive node dissections are still experimental and, if done, they should be carried to the level of the diaphragm In spite of occasioning a two-month delay, he also advocates a full course of irradiation (4000–5000r between the groin and the tenth dorsal vertebra over a four to five-week period) This is given before node dissection is performed on the patient with known metastases However, Hudson,[36] belongs to the school of thought that maintains that irradiation should not be given until after the node dissection has been performed

Cox,[34] and Merren, Vest and Lupton[37] both favor, for radioresistant tumors, simple orchiectomy followed by roentgen therapy, but Kimbrough and Cook[38] recommend radical orchiectomy* without radiotherapy Lewis[39] has given up to 5000r where there was positive retroperitoneal involvement on prior node dissection He cites five patients, with proved metastases on dissection, who died up to three years later from the complications of radiotherapy These patients showed no evidence of recurrence at autopsy He agrees with the generally accepted concept that it is not necessary to irradiate the inguinal region after radical surgery

Dean maintains that when palliation is indicated radiotherapy is the method of choice, and emphasizes that the dose be confined to that which is unlikely to

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* Orchiectomy with high ligation of the cord plus retroperitoneal node dissection

[33] Benjamin, J A N Y State J Med , 56 266, 1956

[34] Cox R Brit J Urol 26 350, 1954

[35] Dean, A L J Urol 76 439 1956

[36] Hudson P L Testicular carcinoma Read before the Hartford County Medical Society, Hartford Conn March 4 1957

[37] Merren, D D , Vest S A and Lupton Jr C H J Urol , 65 128, 1951

[38] Kimbrough, J C and Cook, Jr , F E J A M A , 153 1436, 1953

[39] Lewis, L G J Urol 69 841 1953

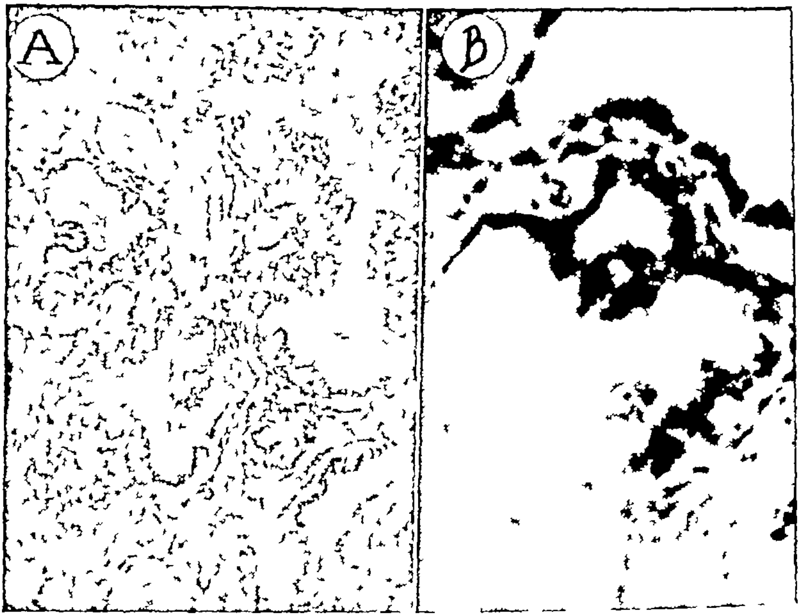

Fig 4 Case 2 Photomicrographs A, low power B, high power

Table 1 *Age distribution of the series*

Age in Mos	0–11	12–23	24–35	36–47	48–59	60–71	72–83	108–119	120–131
No of patients	3	13	6	1	2	2	1	1	1

Table 2 *Minimum reported survival time of 26 patients followed*

Ten Patients with Metastases at Initial Surgery

Survival in Yrs	0–0.5	0.5–1	1–1.5
No of patients	7	2	1

Sixteen Patients without Metastases at Initial Surgery

Survival in Yrs	0–0.5	0.5–1	1–1.5	3–3.5	3.5–4	5–6	6–7	10–11	13–14
No of patients	5	3	2	1	1	1	1	1	1

Lewis[32] have calculated an increased malignancy rate of all testicular tumors in undescended testes of 13 and 22 times, respectively

Table 2 shows that all ten deaths reported occurred within eighteen months of the time of initial surgery, regardless of the type of therapy Nine of these had metastases when first treated, and Doyle[18] only states that no palpable

[32] Lewis L G J Urol 59 763, 1948

who survived more than three years were less than 24 months old it still seems unsafe to conclude rather than postulate a relationship between age and survival time within the childhood years

SUMMARY

A review of the reported instances of embryonal carcinoma of the testis in children has been made and two of the author's patients have been added to make a total of 30 reported cases The purpose of the review is to accumulate data on which a physician could base his decision with regard to treatment and prognosis, there being no such study available Where conclusions of statistical validity could not be drawn, data were presented from the disease as it is seen in adults There is a suggestion that the disease in children differs somewhat from that seen in adults in that children and particularly those under two years of age, may have a more favorable prognosis

For their suggestions and criticism I would like to express my appreciation to Drs C H Neuswanger and J Shearer of the Department of Urology Dr J James of the Department of Radiology and Dr J O Collins of the Department of Pathology

bring injury during the expected life of the patient Isolated pulmonary metastases are treated by Phillips and Dargeon with radiotherapy, and by Kimbrough and Cook with resection

It is of interest to note accounts of the trial of estrogens,[39] testosterone[40] and nitrogen mustard[41] in the treatment of metastatic tumors of the radioresistant type

Because of the known variation in response to radiotherapy, the literature places some emphasis on basing the choice of treatment on the microscopic findings (seminoma and adult teratoma versus all the other germinal tumors occurring in the testis) Too much reliance can be placed on this,[42] and simple excisional biopsy* is generally given preference to incisional biopsy [36] Incisional biopsy is frowned upon because of the danger of local recurrence, and only one patient in this children's series had this procedure performed,[15] as the patient was terminal In view of all that is being written about what to do after the orchiectomy, it is interesting that in this present review five of the six patients surviving three years or longer had the simple operation, while the other patient had the radical operation and irradiation

PROGNOSIS

Prognosis may be assessed by considering the histologic picture and the presence or absence of metastases The inference of these is well known The significance of the chorionic gonadotrophin elevation has already been considered The presence of tumor cells in the vessels of the cord is an ominous sign, and makes widespread dissemination a probability [27]

The figures for five-year survival in adults, as prepared by Dean, are of particular significance, because his findings are based on a series of approximately three hundred patients with embryonal carcinoma These showed a five-year rate of 35 5 per cent In view of the fact that the previously mentioned mortality rate per 100 survivors is only 2 0 per cent after the third year, for practical purposes the figure 35 5 per cent may be considered to closely approximate the cure rate

On the basis of the same data used by Dean, Dixon and Moore[27] have shown a significant difference between the two-year mortality of patients treated by simple orchiectomy (63 per cent) and with retroperitoneal node dissection in addition (44 per cent) † In this (statistically inadequate) survey of the disease in children the results of simple orchiectomy make one ponder the possibility that the disease is of a different character following puberty Although Phillips and Dargeon, referring to all testicular tumors, state that the prognosis is better in infants than in children, and although all six patients, of the 28 cases reviewed,

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* The term "diagnostic orchiectomy" used by Hudson is appropriately emphatic

† One must bear in mind, however, that no figures are given to show the number of patients who received the radical operation, although they showed no metastases at the time of diagnosis

[40] Parkhurst, E Hormone therapy in testicular tumor Read before a meeting of the New England Section of the A U A, Boston, Mass, Feb 28, 1957

[41] Covill, F J Guy's Hosp Reports, 104 19, 1955

[42] Guilleminet, M and Fournier, P Lyon chir, 44 57, 1949

urethra with resulting trabeculated appearance of the posterior urethra Thus distortion of the posterior urethra is usually the result of fibrotic changes originating in deeper prostatic layers In other instances interstitial inflammation can can be localized in one segment of the prostate and in these cases there is no distortion of the posterior urethra These circumscribed tuberculous areas can be calcified and these calcified areas can be surrounded by essentially normal prostatic tissue

However, if the local resistance is inadequate, instead of healing, caseation can occur, with abscess formation This abscess may eventually break into the posterior urethra or through the prostatic capsule

In rare cases the whole prostate and seminal vesicles may be destroyed by tuberculosis A huge cavity may be formed by the completely liquified, destroyed prostate

There is a healing tendency in tuberculosis even in cases untreated with antituberculous medication The smaller the original tuberculous focus the more complete the healing can be

Noncavitary infiltration and even small cavities may heal with resulting connective tissue defect, and indeed, the healing can be so complete that histologically characteristic tuberculous change may not be seen in the healed connective tissue area [3]

In the more advanced cases—in the pretuberculous drug era—healing occurred, by being walled off from the urinary tract These walled off caseated areas may become eventually calcified or will be surrounded by a calcific wall However, living bacilli may be found in these calcified areas decades later As a matter of fact, these caseated calcified areas within the genitourinary tract, or the caseated calcified tuberculous glands, form a common source of late secondary tuberculous spread

How often healing occurred before the introduction of antituberculous therapy is not well documented Clinically, the unsatisfactory healing tendency was well demonstrated by a review of 60 cases of tuberculosis of the prostate [2] Of these 60 cases 12 had severe and at times uncontrollable frequency, and pain Six had perineal fistulas Two had mild but persistent symptoms most of the time

Auerbach[4] studied 105 cases of prostatic tuberculosis found in autopsied tuberculous patients In 18 of these 105 cases of prostatic tuberculosis there was a perforation of the liquified caseous material into the posterior urethra and in two cases the perforation occurred into the rectum

DIAGNOSIS

Early diagnosis of tuberculous involvement of the genital tract is very difficult and even advanced tuberculous disease may be present without significant urological symptoms Clinical recognition of the tuberculous disease in the genitourinary organs in Medlar's[1] series occurred in only 18 per cent of cases

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[3] Auerbach, O Proof of healing of renal tuberculosis Surg Clinic of North Amer, 20 471–474, 1940

[4] Auerbach, O The pathology of urogenital tuberculosis Internat Clinic, 3 21–61, 1940

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TUBERCULOSIS OF PROSTATE AND SEMINAL VESICLES

ANDREW SPORER AND GORDON OPPENHEIMER

The exact incidence of genitourinary tuberculosis is difficult to ascertain Most data are from select material, usually from hospitals for tuberculosis Even Medlar's[1] data published in 1949 originated from a general hospital, in which a large number of beds is reserved for tuberculous patients In that study Medlar and his associates analyzed 5,424 necropsies performed on males over 16 years of age Tuberculous lesions in the genitourinary tract were present in 3 1 per cent of all necropsy material

In recent years the death rate of pulmonary tuberculosis has fallen, not only in this country, but all over the world It may be presumed, although not actually known, that there has been a decline in genitourinary tract tuberculosis as well Inasmuch as the genital tract involvement is the result usually of early hematogenous spread, with clinical manifestations of the disease appearing decades later, a significant decline of the genital tract involvement cannot be expected in the immediate future This decline will be manifested later, especially if the primary infection will be controlled with effective antituberculous medication

INCIDENCE OF GENTIOURINARY TUBERCULOSIS

Data gleaned from past studies indicate that the involvement of genital organs in patients dying of tuberculosis was 10 to 14 per cent In one series of 736 autopsied male patients who died from tuberculosis and not treated with antituberculous medications, the genital tract was involved in 117 cases[2]

PATHOGENESIS

It is possible for the genital tract to be infected in five ways 1) primary tuberculous infections per urethram, 2) direct extension from neighboring organs, 3) descending infection from the urinary tract, 4) lymphatic spread, 5) early and late hematogenous dissemination

Hematogenous spread accounts for most genital tract involvement This may be the result of several seedings In the prostate the lateral or peripheral part is the more often involved in hematogenous spread In cases of descending infection the disease begins near the prostatic urethra and diminishes toward the periphery

Generally speaking, infection within the genital tract is catarrhal or interstitial Catarrhal infection is usually the result of a nonspecific infection, although in an early stage of tuberculosis, a catarrhal type of infection can occur

With good resistance the tuberculous infection does not progress beyond the interstitial stage If the fibrosis is marked, eventually scar tissue will develop in the prostate This fibrosis may extend to the mucosal surface of the posterior

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Accepted for publication February 28, 1957

[1] Medlar E M , Spain, D M and Holliday R W Post mortem compared with clinical diagnosis of genitourinary tuberculosis in adult males J Urol 61 1078-1088 1949

[2] Sporer, A and Greenberger M Genito urinary tuberculosis Sea View Hosp Bull , 16 95-100 1956

TABLE 1 *Surgical procedures in tuberculosis of the prostate*

	No of Cases
Transurethral prostatectomy	10
Perineal prostatectomy	5
Retropubic prostatectomy	3
Suprapubic prostatectomy	3
	—
	21

TABLE 2 *Results of surgical procedures for tuberculosis of the prostate*

Type of Prostatectomy	No of Cases	Good	Bad	Fair
Transurethral resection	10	3	2	5
Perineal prostatectomy	5	2	3	
Retropubic prostatectomy	3	1		2
Suprapubic prostatectomy	3	1		2

When bladder ulceration occurs as a complication of tuberculosis of the prostate—a not infrequent occurrence—biopsy of the abnormal area may establish the histological diagnosis In several instances at The Mount Sinai Hospital biopsy established such identification (fig 1) No untoward reaction was noted following this procedure

THERAPY OF TUBERCULOSIS OF PROSTATE AND SEMINAL VESICLES

Inasmuch as observations indicated that tuberculosis heals with fibrosis earlier therapy was directed to the promotion of fibrosis around the tuberculous areas

Where conservative therapy failed and where severe urinary symptoms or obstructive uropathy was present surgical intervention was tried Unfortunately the technical difficulties during prostatectomy for tuberculosis of the prostate at times presented virtually insurmountable problems, since not all the tuberculous tissue could be removed and complications of surgery at times were as deadly as the disease for which the surgery was performed Urinary incontinence rectal and perineal fistulas were frequent occurrences

There is no large body of reported data available of patients treated with surgery in the prechemotherapy era In one series of patients operated upon in the decades immediately preceding the present chemotherapy era 21 cases of prostatic tuberculosis were reviewed[2] Of these 21 cases operated upon in nine the tuberculous process was diagnosed before surgery and in six of these nine cases, the surgery was performed for tuberculous involvement of the prostate

The surgical procedures are summarized in table 1

The results of surgical procedures are summarized in table 2

Though there was only one immediate surgical death in this series 2 patients had persistent perineal urinary fistulas after perineal prostatectomy until their death In one patient a rectovesical fistula developed and one was incontinent

Urinary frequency, urgency, pain, bloody ejaculate, hematuria can occur and can be uncontrollable at times The bladder soon becomes involved, tuberculous bladder ulcers develop with fibrosis and contracted bladder The clinical symptoms are exaggerated by secondary infections In instances in which the infection is descending, urinary symptoms probably occur at a much earlier stage

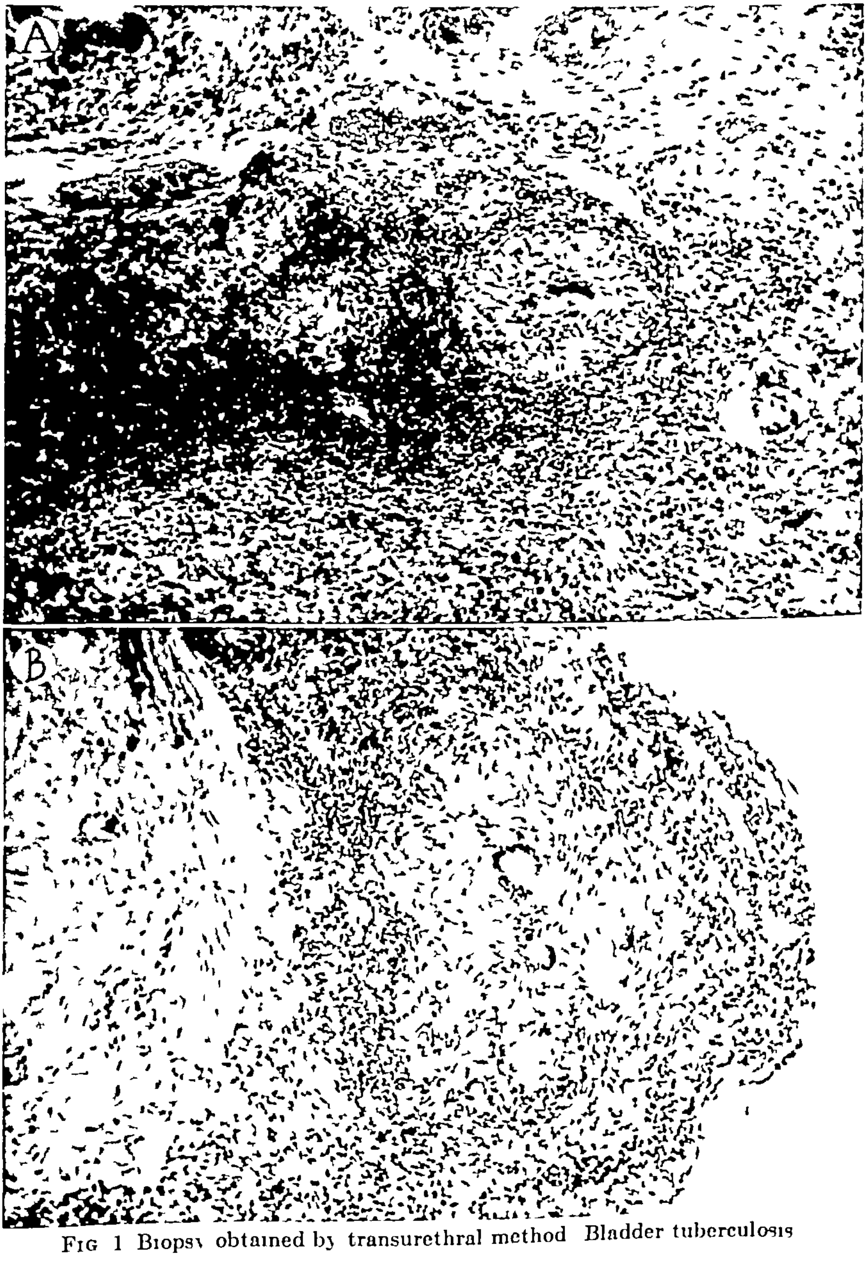

Fig 1 Biopsy obtained by transurethral method Bladder tuberculosis

PAS reactions, if severe, are due to hypersensitivity. Stomach and intestinal symptoms are usually mild and can be overcome with persistence. PAS can cause liver damage and has a definite antithyroid effect as manifested by goiter formation.

Isoniazid has caused toxic nervous system symptoms in some cases. These are usually mild and manifest themselves by paresthesias and peripheral neuropathies. Occasionally it can cause psychosis. Therapy should be discontinued at the earliest sign of cerebral toxicity. Minor side effects like detrusor weakness or diminished sexual potency can occur and have been observed in a few of our cases.

The immediate effect of these antituberculous drugs is the disappearance of toxic symptoms. Fever diminishes and within 10–14 days usually the temperature returns to normal. The patient's general well-being is manifested by increased appetite and increased weight. The healing of the tuberculous process, however, is slow and prolonged, though the clinical improvement is impressive.

Out of 25 cases* of prostatic tuberculosis in which antituberculous drugs were used, 23 are symptomless, have no complaints, and only two have mild frequency on and off—easily controllable with medication.

Clinical improvement does not necessarily mean that the tuberculosis within a genitourinary organ will heal with the same rapidity. In those cases of prostatic tuberculosis where fibrous or calcified nodules were present before therapy, we have not observed anatomical change any time during or after the therapy. No definite prostatic nodule ever becomes smaller or softer. Though we never see any improvement in these nodules, we know that histological improvement can occur in fibrocaseous areas in case of pulmonary tuberculosis. These unchanged areas within the prostate indicate that the healing of the advanced fibrotic and calcified areas still today will heal—by these areas being walled off from the rest of the healthy tissues.

How often will the tuberculosis bacillus disappear from these areas is not known. Living tubercle bacilli in pulmonary lesions may be found years after intensive therapy.[5]

Though the nodules may not change and though virulent bacilli may be found months after therapy began, there is indication that the pathogenicity of these bacilli is modified. Arne Lind[6] described a case after isoniazid therapy where the bacilli became resistant to isoniazid. When these bacilli were injected into guinea pigs they were not pathogenic any more although the guinea pigs were injected 3–4 months after the cessation of therapy. This nonpathogenicity of tubercle bacilli was observed even 16 months after the cessation of therapy.

If caseation is progressive or if it causes obstructive uropathy or severe urinary symptoms, surgery might be necessary in occasional cases. Hypertrophy of the prostate with tuberculous areas in the prostate might require prostatectomy.

Auerbach[4] noted that in 7 cases out of 100 tuberculous prostates the tubercuafter transurethral prostatectomy Two patients who had retropubic prostatectomy received streptomycin postoperatively for a short time, but had no other antituberculous type of medication

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[5] Hobby, G., Auerbach, O., and Small, L.: Effect and degree of healing upon persistence of tubercle bacilli within pulmonary lesions. Am. Rev. Tuberc. 72, 350, 1955.

[6] Lind, Arne: Ein Fall von mit Isonikotinsäure hydrazid behandelter Urogenitaltuberkulose mit für Meerschweinchen apathogenen Tuberkelbazillen. Urologia Internationalis 1, 63–65, 1955.

This experience would indicate that the result of both surgical-medical treatment of tuberculosis of the prostate was unsatisfactory in the pre-chemotherapy era The introduction of antituberculous medication has almost incredibly modified and improved our therapeutic results

The drugs most frequently used in genitourinary tuberculosis are streptomycin, dyhydrostreptomycin, isoniazid, para-aminosalycilic acid

The mode of action of these drugs is not known It is believed that some of these act by competitive interference with an essential metabolite of the bacterium This competitive interference is probably the effective factor in isoniazid therapy

The effect of para-aminosalycilic acid might be different There is some indication that this substance interferes with the oxygen consumption of the tubercle bacilli and thereby inhibits bacterial growth

The tubercle bacilli are usually intracellularly located within a macrophage The easier these drugs can penetrate the macrophage, the more effective their action should be

Isoniazid can penetrate even caseous lesions This ability to penetrate tissue is poor in case of streptomycin and hardly existent with PAS

It has been observed that after the onset of therapy there is perifocal clearing This clearing, of course, prevents fibrosis which was the aim of urological therapy The prevention of this fibrosis is more marked with isoniazid therapy, in which increased vascularity also occurs Streptomycin used alone will not diminish the formation of fibrosis and the tuberculous area is rather avascular

The natural resistance of the host increases the efficacy of medication Whatever direct or indirect action these drugs have, their action is increased by the body's many unknown defense mechanisms Where the body resistance is low, the spread of the disease is usually greater in spite of antituberculous medication

All these drugs should be applied with careful observation of the patient as toxic manifestation can occur

The damage to the eighth nerve from streptomycin or dihydrostreptomycin is well known The hearing impairment is usually permanent and rarely improves even if the medication is stopped A careful check on the eighth nerve function should always be made and audiometric tests should be made at the slightest symptom

If the moderate doses which seem to be adequate in genitourinary tuberculosis are used, the complications from streptomycin therapy are rare Streptomycin, however, has a nephrotoxic effect and patients with diminished kidney function will eliminate streptomycin slowly The blood level can be very high in impaired kidneys if the usual dosage is used Inasmuch as several cases of encephalopathies have been described from the use of streptomycin, these high blood levels should be avoided The toxic reactions usually occur in the third or fourth week of therapy, but can occur at any time

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Auerbach[4] noted that in 7 cases out of 100 tuberculous prostates, the tuberculosis was associated with prostatic adenoma We observed three cases where the removed hypertrophied prostate contained tuberculous areas

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[5] Hobby G Auerbach, O and Small L Effect and degree of healing upon persistence of tubercle bacilli within pulmonary lesions Am Rev Tuberc 72 386 1955

[6] Lind Arne Ein Fall von mit Isonikotinsäure hydrazid behaltender Urogenitaltuberkulose mit für Meerschweinchen apathogenen Tuberkelbazillen Urologia Internationalis 1 63–65 1955

While the number of cases requiring surgery is much smaller in most centers, a rather large series of cases requiring surgical intervention was published recently by Semb [7] The indications for surgery are not mentioned in his publication He reported 25 cases of prostatic tuberculosis with transurethral prostatic resection He stated that there was no serious complication in any one of these cases and the posterior urethra did look essentially normal after surgery All these cases were treated with antituberculous therapy simultaneously

In some cases of localized disease, partial prostatectomy would appear to be of value, one such operation was done by one of us (G O) and seems worth noting in detail since no previous report of this procedure has been made

CASE REPORTS

Case 1 A 45-year old man with urinary frequency and urgency was seen in April 1949 Examination revealed a hard, nodular area in the prostate Acid phosphatase test, chest x-ray and intravenous pyelogram were essentially negative Sedimentation rate was 8 mm

To exclude carcinoma a perineal exploration was performed and a caseated tuberculous nodule found in the right lateral lobe of the prostate A smaller tuberculous nodule was found in the left lateral lobe Extensive excision of both lateral lobes was performed without entering the urethra The operation was uneventful, the wound was drained only with a small Penrose drain The patient left the hospital on the twelfth postoperative day with an almost completely healed wound The patient took 2 gm streptomycin daily for 6 weeks The wound was firmly healed at the end of the third week and the patient had no complaints or symptoms Postoperatively, for a time, the patient complained of impotence, but normal sexual activity returned in about 18 months postoperatively

Histological examination of the removed prostate revealed tuberculosis with extensive caseation In 1953 the urine examination was positive for tuberculosis and genitourinary studies revealed tuberculous involvement of the left kidney This time the patient received prolonged and intensive antituberculous medication with combination of several antituberculous agents The urine became negative in 1954 and has remained negative since

The conservative management of a patient is well illustrated in case 2, probably the first urological patient to be treated with isoniazid

Case 2 B L , a 36-year-old white man, was first seen in January 1952 He gave a history of right epidydimitis in 1950 Because of mild urinary symptoms, burning and frequency, after treatment with penicillin he received prostatic massages for several months He felt well until December 1951, when left epididymitis developed In spite of penicillin therapy the swelling persisted He had low grade temperature, but no urinary symptoms or urethral discharge

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[7] Semb, Carl The selective principle in the treatment of urogenital tuberculosis Partial resection of the kidney and of the ureter Urologia Internationalis, 1 359-395, 1955 (Dr Hoeg-Dep 111 Ullevaal)

At the time of the first examination the left epididymis was markedly enlarged and thickened The right epididymus was also thickened and indurated Rectal examination revealed a firm prostate with a hard nodule in the right lobe and a tiny hard nodule in the left lobe A small nodule was felt in the right seminal vesicle The left seminal vesicle was firm but had no palpable nodule in it X-ray showed no calcification in the prostate An intravenous pyelogram showed excellent kidney function bilaterally with normal kidneys, calyces and ureters The concentrated urine sediment smear and culture were positive however for tuberculosis

In January 1952, antituberculous medication was begun using isoniazid The patient received 400 mg isoniazid and ½ gm streptomycin daily In spite of medication a huge fluctuating mass developed in the left scrotum and an epididymal abscess eventually broke through the scrotal skin

The patient was hospitalized at the Barnert Memorial Hospital, Paterson, N J and on March 10, 1952 an epididymo-orchiectomy was performed The ductus deferens was removed to the external ring Isoniazid and streptomycin therapy was maintained and the patient discharged on the seventh postoperative day with a healed scrotal wound

Histological diagnosis by Dr J Churg Tuberculous epididymitis with orchitis and abscess formation

The patient received 12 gm PAS and 300 mg isoniazid daily and 1 gm streptomycin biweekly for 1 year In 1954 and in 1955 he received again isoniazid and PAS for three months His urine was always negative He had bloody ejaculate on and off for 6 months after therapy began His general condition is excellent He never had any urinary complaints Examination in September 1956 revealed that the left prostatic lobe was smooth and soft The right lobe contained the unchanged big and small nodules and for the first time x-ray showed calcification within the right prostatic lobe One culture from the ejaculate was done in 1953 and was reported negative

In this case, in the left lobe the healing occurred by replacement fibrosis in a small area and the probably catarrhal type of inflammation cleared completely In the right lobe healing will occur with demarcating calcification Cystoscopically the prostatic urethra was always normal

These cases clearly illustrate the type of management we prefer to recommend today It was noted in the past that the calcified areas within the genital tract form a common source for late hematogenous spread [1] Since the introduction of antituberculous therapy we have not observed any evidence of late spread from these tuberculous nodules

Optimal therapy includes a combination of antituberculous drugs No drug should be used alone since the development of drug resistant strains is frequent in single-drug therapy If possible three drugs should be used at the same time, though we may alternate these drugs The therapy should be maintained for at least 12–18 months and can be repeated several times for a shorter or longer interval if so desired We recommend at least six months of sexual abstinence Until further evidence will demonstrate that patients can be successfully treated on an ambulatory basis, we still recommend that six months' rest should accompany the medical management of patients

The prognosis is good in early cases with hope of *restitutio ad integrum* In late fibrotic or calcified cases the medical management should be satisfactory in the great majority of cases but healing probably will occur with these areas being walled off from normal prostatic tissues

Surgery is indicated only in cases of uncontrollable progression or in cases of obstructive uropathy The type of surgical procedure will have to be decided in every case individually, depending upon the localization of the disease If partial prostatectomy is feasible it seems to us to be a procedure of choice

SUMMARY

The medical and surgical management of prostatic tuberculosis in the pre- and post-tuberculous medication era is reviewed

The result of medically and surgically treated patients is discussed Suggested therapy is outlined for genital tuberculosis

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CHANGES IN SERUM ACID PHOSPHATASE LEVELS CONSEQUENT TO PROSTATIC MANIPULATION OR SURGERY*

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The determination of serum acid phosphatases was originally thought to be a specific diagnostic test for metastasizing carcinoma of the prostate.[1] It has since become apparent that many cases of metastatic carcinoma do not have elevated serum acid phosphatase levels.[2] On the other hand, elevated values have been found following manipulation of noncancerous prostates.[3, 4] In spite of these limitations the method is valuable and widely used as a diagnostic test. It has also assumed an important role as a tool to control hormone therapy when estrogen treatment is initiated in cases of prostatic neoplasm. The change in serum acid phosphatases is interpreted as a measure of the effectiveness of the hormone treatment.

In view of the importance that is attached to the determination of the serum enzyme values in carcinoma of the prostate, we have studied how they are influenced by operative procedures and manipulations as we perform them daily on patients with prostatism.

MATERIALS AND METHODS

The experimental series consists of 85 patients undergoing transurethral resection (TUR), 10 patients of advanced age with early prostatism or nonrelated diseases who were selected for prostatic massage and an additional 10 cases who underwent open surgery of the prostate or had transurethral surgery for a nonprostatic disease. Blood samples were taken immediately prior to the surgery or massage and at 30 minutes, 60 minutes, and 24 hours thereafter. The normal fluctuation in serum acid phosphatases (SAP) was determined by doing repeated tests with blood samples from 5 normal young men.

Serum phosphatases were determined colorimetrically according to the method for phosphorus by Fisk and Subbarow with Bodansky's modification.[5, 6]

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[1] Gutman, E. B., Sproul, E. E. and Gutman, A. B.: Significance of increased phosphatase activity of bone at the site of osteoblastic metastasis secondary to carcinoma of the prostate gland. Am. J. Cancer, 28: 485–495, 1936.

[2] Nesbit, R. M. and Baum, W. C.: Serum phosphatase determination in diagnosis of prostatic cancer, review of 1,150 cases. J.A.M.A., 145: 1321–1324, 1951.

[3] Hock, E. and Tessier, R. N.: Elevation of serum acid phosphatases following prostatic massage. J. Urol., 62: 488–491, 1949.

[4] Stewart, C. B., Sweetser, T. N. and Delory, G. E.: Case of benign prostatic hypertrophy with recent infarcts and associated with high serum acid phosphatase. J. Urol., 63: 128–131, 1950.

[5] Fiske, C. H. and Subbarow, Y.: The colorimetric determination of phosphorus. J. Biol. Chem., 66: 375–400, 1925.

[6] Bodansky, A.: Phosphatase studies. II. Determination of serum phosphatase. Factors influencing the accuracy of the determination. J. Biol. Chem., 101: 93–105, 1933.

RESULTS

Normal variations Each of 5 normal young men had serum acid phosphatase values below 0 5 Bodansky units With repeated samples tested at 2-hour intervals, insignificant variations occurred, but no value extended into the abnormal range, above 0 5 units (fig 1)

Variations caused by prostatic massage Within one hour following prostatic massage the average group SAP value rose from the normal range to a level of 0 75 units All ten cases had premassage levels below 0 5 units while after the massage six had risen above this value, which is usually considered as the upper normal limit At the end of 24 hours the average value for the ten cases had returned to normal (fig 2)

Variations with open prostatic surgery or transurethral bladder surgery All patients in this group had preoperative SAP values below 0 5 units There was a small elevation in the group average value at 30 minutes postoperatively but not above the upper normal limit Two of the cases responded to the surgery with increases in SAP slightly above the range considered normal At one hour post operatively, however, these two cases returned to normal and at 24 hours the group average was essentially the same as preoperatively (fig 3)

Variations with transurethral resection of benign prostatic hypertrophy (BPH) In the course of the investigation we noted that the amount of tissue resected had a significant bearing on the SAP variations We have, therefore, presented the results classified according to the amount of tissue resected (fig 4)

BPH resections less than 15 gm In this group of 17 cases all preoperative SAP values were below 0 5 Bodansky units At one hour after surgery the average value was above the normal limit, 65 per cent of the cases had elevated levels but most of these were between 0 5 and 1 0 units Only two cases had SAP values above 2 0 units During the first postoperative day the group average returned to normal, though slightly higher than the preoperative average value

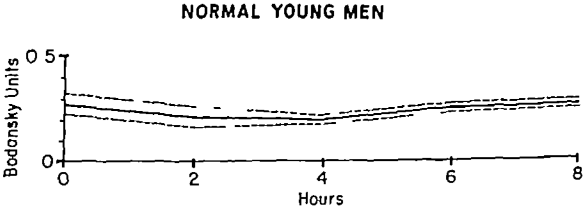


FIG 1 Dotted lines are upper and lower limits, solid lines, group averages

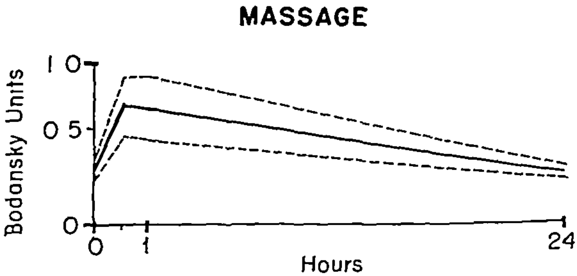
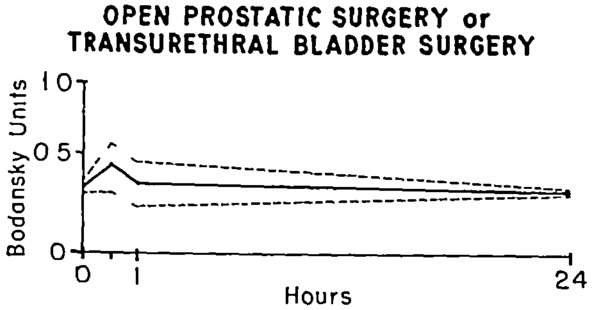


FIG 2 Dotted lines are upper and lower limits, solid lines, group averages



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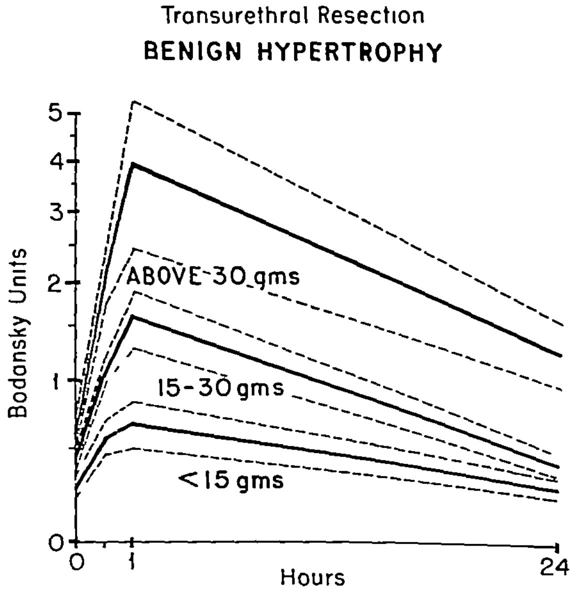

FIG 4 Dotted lines are upper and lower limits, solid lines, group averages

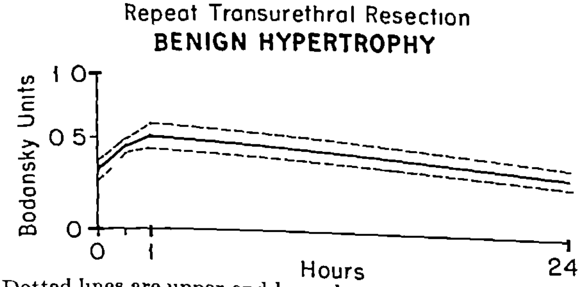

FIG 5 Dotted lines are upper and lower limits, solid lines, group averages

BPH resections between 15 and 30 gm The average SAP level for these 24 cases was below 0 5 units before surgery but a few of the individuals were above the normal range At one hour after surgery, however, all but three of the cases were well above the normal limit and the group average had risen to 1 5 units Nevertheless, within 24 hours the group average returned to the normal range

BPH resections above 30 gm This group included 15 cases of which 12 had initial SAP values slightly above 0 5 units The preoperative group average value was 0 6 units Following resection, there was a sharp rise with 20 per cent of the cases attaining levels above 5 0 units At 24 hours the average SAP value was still markedly elevated

Variations with repeat TUR of BPH This group included 10 patients with benign prostatic hypertrophy who underwent a repeat TUR within two weeks following a previous resection The preoperative average value was in the normal range There was a slight elevation to 0 5 units at one hour after surgery but the

TABLE 1 *Per cent of cases with rise of SAP following TUR of BPH*

Status	No of Patients	<0 5* (Normal) % Cases	Elevation Above			
			0 5 % Cases	1 0 % Cases	2 0 % Cases	5 0 % Cases
Controls (open surgery)	10	50 0	50 0			
BPH						
Repeat TUR	10	50 0	30 0	20 0		
<15 gm	17	35 0	47 1	5 8	11 7	
15–30 gm	24	12 5	25 1	47 7	12 5	8 3
>30 gm	15		13 3	40 0	26 6	20 0

* Bodansky units

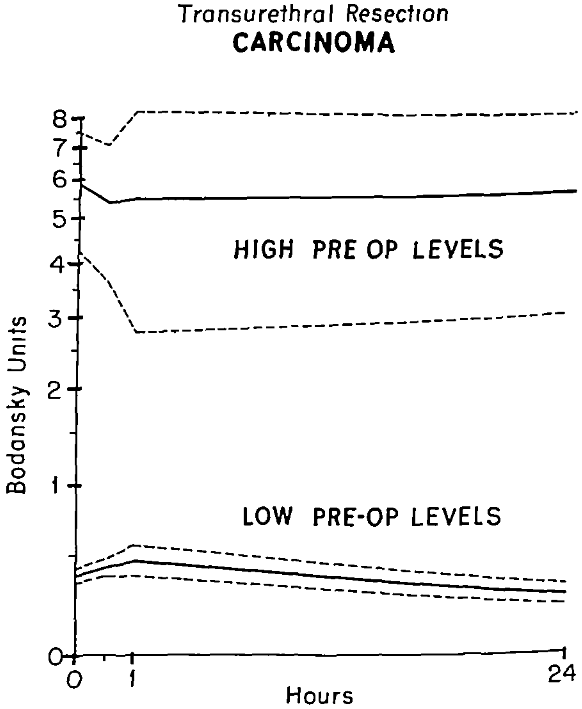

FIG 6 Dotted lines are upper and lower limits, solid lines group averages

group value then returned to 0 3 units at 24 hours It is significant to note that half of the cases did not have a rise in SAP level above the upper normal limit (fig 5)

Summarizing the results of resection in cases of benign prostatic hypertrophy, the postoperative elevation in SAP was greatest when a large amount of tissue was resected (the largest glands) and the least effect occurred in cases where a prior resection had taken place within two weeks These observations are expressed in table 1, which indicates the percentage of the cases in each group which had postoperative increases of various degrees

Variations with TUR of prostatic carcinoma The last group of patients to be considered are those who underwent transurethral resection for carcinoma of the prostate These have been classified according to preoperative SAP levels Fourteen cases had initial SAP values within the normal range This group showed the least postoperative change in SAP of all the experimental groups There was a slight rise at one hour after the surgery, but the over-all change at the end of 24 hours had been negligible The six carcinoma cases with high initial SAP values also showed negligible SAP variation in the 24 hours following resection (fig 6)

DISCUSSION

With a procedure which permits the entrance of vesical contents into the venous system, as may occur during TUR, the passage of stored prostatic secretion into the circulation is just as likely The alteration of SAP levels as a consequence of the entrance of prostatic secretion into the bloodstream is certainly dependent to some extent on operative technique, operating time, and condition of the vascular system, but the primary factor must be *the amount of stored secretion available* This is determined principally by the functional status of the gland, but also by its histologic structure and size Hypertrophy of the prostate, although characterized by a variety of histological pictures, generally shows dilated acinal spaces with some secretory epithelium[7] The cancerous gland generally has microacinar or solid cord structure and the epithelium does not show the typical functional characteristics seen in the normal prostate The important general situation, however, is an increase in the canalicular space in BPH and a decrease in carcinoma Histochemical studies have elucidated an additional difference between the two tissue types, regarding the distribution of acid phosphatase While the enzyme is present in both the carcinomatous and benign glands, in the former it is found intracellularly,[8, 9] and in the latter it is extracellularly stored in the acini Hence, it seems likely that during resection of a BPH, a large quantity of stored secretion can be liberated into the vesical contents and may be carried into the bloodstream Since the acid phosphatase of carcinomatous tissue is enclosed as intracellular material, mainly, it is not

liberated profusely during the operation so that entrance into the circulation does not occur This difference could be confirmed in the following simple experiment, which will be reported in detail elsewhere Benign hyperplastic tissue obtained by partial prostatectomy was thinly sectioned and the slices washed in saline The same procedure was performed with the cancerous portion of a prostate obtained by total prostatectomy From the supernatant fluid of the benign adenoma one-third of the total enzyme content was recovered while from the carcinoma only a small percentage appeared in the supernatant fluid

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[8] Gomori G Distribution of acid phosphatases in the tissues under normal and pathologic conditions Arch Path **32** 189-199 1941

[9] Downey M Hickey B and Sharp M E The acid phosphatase content of the enlarged and malignant prostate gland with some observations on histopathology as revealed by Gomori s staining Brit J Urol **26** 160, 1954

In each prostate different stages of pathologic deterioration may exist at the same time so that an entire gamut of functional abnormalities may be operating simultaneously Hence, the clear-cut difference we have observed between these two groups is surprising This may have been because our series of cases represents an unexpected uniformity in regard to histologic structure All carcinoma patients undergoing TUR were advanced cases, probably having almost solid carcinomas

The effect of altered conditions governing the entrance of prostatic fluid into the bloodstream has been observed in our series Patients with recurrent benign prostatic hypertrophy who have undergone partial prostatectomy at least six months prior to the study showed generally the typical behavior of their group with regard to the SAP changes This indicates that with tissue regeneration a functional restitution occurred In contrast to this, the group of individuals in whom the repeat operation was performed within a short time (1 to 2 weeks) after the first, did not show a significant increase in SAP levels One can assume that the secretion in the residual tissue has been almost completely destroyed or changed by electrocoagulation and new secretion has not yet been produced As an additional causative factor for the failure of an SAP rise corresponding to the anatomical structure and the weight of the specimen, one must keep in mind the possible blockage of the circulatory pathway due to thrombosis following the original operation Blockage of the venous plexus by thrombosis, cancerous tissue or other obstructions would inhibit the rise in SAP levels while an extensive opening of the venous channels, high pressure of the irrigation fluid, and long duration of the resection would be contributory to an increase Individual examples of these situations occurred There was no constant relationship between the age of the patient and his SAP level changes with transurethral prostatic resection, nor was there a demonstrable influence by the mode of anesthesia

The elevated initial values found in the group with the largest benign glands are most likely the result of manipulations prior to the operation, before the initial blood sample was drawn That source of error could not be avoided within the routine preoperative measures in a teaching hospital It has been definitely proven that there were no cases of carcinoma within this group

CONCLUSIONS

During transurethral resection prostatic secretion may enter the bloodstream with a consequent rise in serum acid phosphatases The amount of transfer de pends on several factors, but primarily on the size and functional status of the gland The greatest SAP changes after transurethral resection have been observed in the patients with large hyperplastic glands There is only a slight effect on the enzyme content of the serum when prostatic carcinomas are resected Structurally, the hyperplastic gland contains an abundance of canalicular space with a large storage of prostatic fluid available for entrance into the bloodstream coincidental with the surgery Carcinomatous tissue, on the other hand, has frequently lost the acinal structure and while the functional capacity to produce phosphatases remains, the enzyme is located intracellularly and does not readily enter the circulatory system during resections

SUMMARY

Serum acid phosphatase levels have been studied with respect to fluctuations occurring as a result of prostatic massage or surgery

Following massage there is a rise in SAP levels frequently into the range usually considered pathologic At 24 hours after the massage the values have returned to normal

When benign hyperplastic glands are resected transurethrally there is a subsequent rise in the SAP values, with the increase directly proportional to the size of the gland and the amount of tissue resected Repeat resections of hyperplastic glands, performed within 2 weeks of a previous one, fail to have as marked an effect on the SAP values

Resection of carcinomatous glands does not cause a significant rise in the SAP levels consequent to the operation

It is concluded that the difference in the changes of SAP levels after transurethral resection of pathologically different prostates results from certain functional and histologic characteristics unique for each type of tissue

liberated profusely during the operation so that entrance into the circulation does not occur This difference could be confirmed in the following simple experiment, which will be reported in detail elsewhere Benign hyperplastic tissue obtained by partial prostatectomy was thinly sectioned and the slices washed in saline The same procedure was performed with the cancerous portion of a prostate obtained by total prostatectomy From the supernatant fluid of the benign adenoma one-third of the total enzyme content was recovered while from the carcinoma only a small percentage appeared in the supernatant fluid

In each prostate different stages of pathologic deterioration may exist at the same time so that an entire gamut of functional abnormalities may be operating simultaneously Hence, the clear-cut difference we have observed between these two groups is surprising This may have been because our series of cases represents an unexpected uniformity in regard to histologic structure All carcinoma patients undergoing TUR were advanced cases, probably having almost solid carcinomas

The effect of altered conditions governing the entrance of prostatic fluid into the bloodstream has been observed in our series Patients with recurrent benign prostatic hypertrophy who have undergone partial prostatectomy at least six months prior to the study showed generally the typical behavior of their group with regard to the SAP changes This indicates that with tissue regeneration a functional restitution occurred In contrast to this, the group of individuals in whom the repeat operation was performed within a short time (1 to 2 weeks) after the first, did not show a significant increase in SAP levels One can assume that the secretion in the residual tissue has been almost completely destroyed or changed by electrocoagulation and new secretion has not yet been produced As an additional causative factor for the failure of an SAP rise corresponding to the anatomical structure and the weight of the specimen, one must keep in mind the possible blockage of the circulatory pathway due to thrombosis following the original operation Blockage of the venous plexus by thrombosis, cancerous tissue or other obstructions would inhibit the rise in SAP levels while an extensive opening of the venous channels, high pressure of the irrigation fluid, and long duration of the resection would be contributory to an increase Individual examples of these situations occurred There was no constant relationship between the age of the patient and his SAP level changes with transurethral prostatic resection, nor was there a demonstrable influence by the mode of anesthesia

The elevated initial values found in the group with the largest benign glands are most likely the result of manipulations prior to the operation before the initial blood sample was drawn That source of error could not be avoided within the routine preoperative measures in a teaching hospital It has been definitely proven that there were no cases of carcinoma within this group

CONCLUSIONS

During transurethral resection prostatic secretion may enter the bloodstream with a consequent rise in serum acid phosphatases The amount of transfer depends on several factors, but primarily on the size and functional status of the gland The greatest SAP changes after transurethral resection have been observed in the patients with large hyperplastic glands There is only a slight effect on the enzyme content of the serum when prostatic carcinomas are resected Structurally, the hyperplastic gland contains an abundance of canalicular space with a large storage of prostatic fluid available for entrance into the bloodstream coincidental with the surgery Carcinomatous tissue, on the other hand, has frequently lost the acinal structure and while the functional capacity to produce phosphatases remains, the enzyme is located intracellularly and does not readily enter the circulatory system during resections

SUMMARY

Serum acid phosphatase levels have been studied with respect to fluctuations occurring as a result of prostatic massage or surgery

Following massage there is a rise in SAP levels frequently into the range usually considered pathologic At 24 hours after the massage the values have returned to normal

When benign hyperplastic glands are resected transurethrally there is a subsequent rise in the SAP values, with the increase directly proportional to the size of the gland and the amount of tissue resected Repeat resections of hyperplastic glands, performed within 2 weeks of a previous one, fail to have as marked an effect on the SAP values

Resection of carcinomatous glands does not cause a significant rise in the SAP levels consequent to the operation

It is concluded that the difference in the changes of SAP levels after transurethral resection of pathologically different prostates results from certain functional and histologic characteristics unique for each type of tissue

liberated profusely during the operation so that entrance into the circulation does not occur This difference could be confirmed in the following simple experiment, which will be reported in detail elsewhere Benign hyperplastic tissue obtained by partial prostatectomy was thinly sectioned and the slices washed in saline The same procedure was performed with the cancerous portion of a prostate obtained by total prostatectomy From the supernatant fluid of the benign adenoma one-third of the total enzyme content was recovered while from the carcinoma only a small percentage appeared in the supernatant fluid

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The effect of altered conditions governing the entrance of prostatic fluid into the bloodstream has been observed in our series Patients with recurrent benign prostatic hypertrophy who have undergone partial prostatectomy at least six months prior to the study showed generally the typical behavior of their group with regard to the SAP changes This indicates that with tissue regeneration a functional restitution occurred In contrast to this, the group of individuals in whom the repeat operation was performed within a short time (1 to 2 weeks) after the first, did not show a significant increase in SAP levels One can assume that the secretion in the residual tissue has been almost completely destroyed or changed by electrocoagulation and new secretion has not yet been produced As an additional causative factor for the failure of an SAP rise corresponding to the anatomical structure and the weight of the specimen, one must keep in mind the possible blockage of the circulatory pathway due to thrombosis following the original operation Blockage of the venous plexus by thrombosis, cancerous tissue or other obstructions would inhibit the rise in SAP levels while an extensive opening of the venous channels, high pressure of the irrigation fluid, and long duration of the resection would be contributory to an increase Individual examples of these situations occurred There was no constant relationship between the age of the patient and his SAP level changes with transurethral prostatic resection, nor was there a demonstrable influence by the mode of anesthesia

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CONCLUSIONS

During transurethral resection prostatic secretion may enter the bloodstream with a consequent rise in serum acid phosphatases The amount of transfer de-

Surgery must frequently be resorted to in patients whose severe spasticity fails to respond to conservative treatment Among the surgical measures one may employ tenotomy, peripheral neurectomy subarachnoid alcohol injection anterior or posterior or combined rhizotomy and "rootlet" rhizotomy Surgical procedures are usually not resorted to within a year after injury in order to allow for a possible spontaneous return of function Satisfactory bladder and sex function are contraindications to subarachnoid alcohol injection or to lumbosacral rhizotomy unless the need for the relief of the severe spasticity is extremely urgent

Since spasticity frequently subsides in severity after a varying length of time and since surgical measures are at times contraindicated the ideal solution of the problem would be medical control or amelioration of spasticity

Prostigmine and tubocurarine have been tried and abandoned as ineffective Mephenesine intravenously has been shown experimentally to cause relaxation of skeletal muscle Its effect however is very short lasting and oral administration of the drug has proved useless Funderburk and Woodcock[3] and Marsh[4] have reported their experiments with 2-amino-5-chlorobenzoxazole (McN-485) which gave longer relaxation than mephenesine and had the advantage of oral administration Favorable reports of treatment of spasticity by zoxazolamine (flexin)[5, 6] caused us to undertake an investigation of its effectiveness in relieving spasticity in cases of spinal cord injury Our method consisted of clinical evaluation of the degree of spasticity before and after the treatment by the doctor, the therapist and the patient Its effect on bladder spasticity was evaluated by cystometric examinations before and after therapy Three paraplegic and three quadriplegic patients were treated with 500 mg flexin q i d with length of treatment varying from one week to more than a month One of the paraplegic patients and one of the quadriplegic patients were later treated with a higher dosage 750 mg flexin q i d

In the latter two patients there were symptoms of light-headedness on the higher dosage and the quadriplegic patient also complained of marked weakness No other evidence of toxicity was found during this clinical investigation

Clinical evaluation showed no evidence of lessened spasticity of the skeletal muscles after the therapeutic trial The cystometric studies revealed no essential difference between the pretreatment and post-treatment curves While one may perhaps question the inclusion of the spastic bladder in this study because the effect of the drug on smooth muscle may differ from that on skeletal muscle

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[3] Funderburk W H and Woodcock R T Effects of 2 amino-5 chlorobenzoxazole on the central nervous system Fed Proc 14 341 1955

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[5] Amols W Clinical experience with a new muscle relaxant zoxazolamine J A M A 160 742-745 1956

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EVALUATION OF THE EFFECT OF ZOXAZOLAMINE (FLEXIN) ON SPASTICITY

ANDOR A WEISS, GEORGE B D'ORONZIO AND ALFRED EBEL

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The treatment of severe spasticity still offers one of the major challenges in the care of patients suffering from spinal cord injury

In individuals whose level of injury is above the conus, after the spinal shock has subsided, spasticity may be evoked by any stimulus received in the distal segment of the spinal cord, although the patient may not be aware of these stimuli They may arise from urinary infections or calculi, decubitus ulcers, ill fitting braces, and at times even from calluses or ingrown toe nails The strong contractions set up in one group of muscles may act as further stimuli causing spasticity in other groups of muscles

When the spasticity is only of mild to moderate degree, this is not harmful Quite to the contrary, it is beneficial because it may prevent disuse atrophy of the muscles below the level of the lesion Such patients do not require any treatment for spasticity

Frequently, however, the spasticity may be so severe as to interfere with the patient's sleep, nutrition and with his rehabilitation At times it may even threaten the patient's life In such cases the predisposing causes mentioned above should be sought out and corrected After these have all been eliminated, many patients still have severe spasticity

Conservative measures of treatment include relaxing the spastic muscles by immersing the patient in a warm Hubbard tank (temperature about 100F), followed by mild passive range of motion exercises While this does benefit some patients temporarily, from a practical point of view it may be difficult to carry out at times In warm weather patients whose thermo-regulatory mechanism is inefficient frequently are unable to tolerate the warm bath In cold weather, on the other hand, when patients have to be moved through drafty halls in a hospital they are frequently subject to upper respiratory infections and for that reason Hubbard tank treatment may have to be stopped Instead of relaxing the muscles, others have tried to exhaust them by the use of electrical stimulation[1, 2] This has afforded temporary benefit, but it is not very effective in marked spasticity The muscles may also be exhausted by early mobilization of patients and having them stand up between parallel bars for as long a period of time as they are able to tolerate The spasticity is reduced in these patients because the exhausted muscles are unable to respond to stimuli reaching them from the distal segment of the spinal cord

Accepted for publication March 18, 1957

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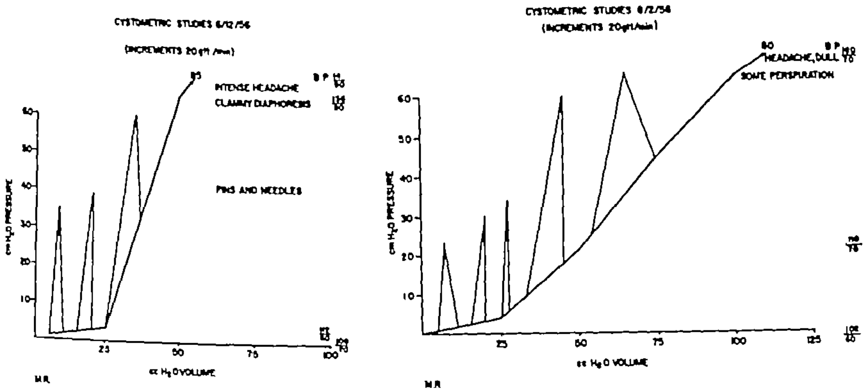


FIG 2

On May 3, 1956 flexin therapy was started with an oral dosage of 500 mg q i d This was continued until May 19, 1956 No subjective improvement resulted, and physical examination revealed no objective evidence of lessened spasticity of the abdominal muscles

On May 21, 1956 two cystometric readings were taken (fig 1) During the first reading, there was a steep gradient to 34 cm of H_2O of intracystic pressure when the bladder was filled to 50 cc At 75 cc capacity sudden voiding contraction occurred with leakage around the catheter At the second trial, the intracystic pressure rose swiftly to 40 cm H_2O at 50 cc filling, with the sharp fluctuations continuing up to 150 cc when the patient voided around the catheter

Comment After 15 days of treatment with 500 mg of zoxazolamine (flexin) q i d , the patient had obtained neither subjective nor objective evidence of relief from the abdominal wall spasticity, and cystometric studies showed no improvement of the bladder spasticity when compared with the pretreatment status

Case 2 M R F , a 19-year-old white man, became a paraplegic as a result of a gunshot wound at level of T-4 on May 15, 1955 A laminectomy performed on the same day showed a fracture of the T-4 and T-5 spinous processes Spasticity appeared soon after injury A bladder stone had to be removed by suprapubic cystolithotomy

Cystoscopic examination on June 19, 1956 revealed a small, spastic bladder of about 100 cc capacity No calculi were found

Flexin 500 mg q i d was started on June 25, 1956 and continued at the same dosage until August 14, 1956

Cystometric study (June 12, 1956) Sharp swings of intracystic pressure with total capacity of 60 cc Severe headaches were experienced at this point The blood pressure was 144/90 and the patient had a voiding contraction See figure 2

August 2, 1956 Again a sharp rise of the intracystic pressure occurred with wide swings and a total capacity of 110 cc At this point the patient had a voiding contraction See figure 2

A cystogram on August 27, 1956 showed no evidence of a reflux this objection is invalid It has been shown that the effect of zoxazolamine is on the polysynaptic pathways, depressing them at the spinal interneuronal level, and having no effect on the motor nerves, myoneural junction or the muscle itself Furthermore, there was no effect shown on the spastic skeletal muscles

The "light-headedness" complained of by the patients on the higher dosage is similar to the suprasegmental sedative effect of the drug during experimental investigation

CASE REPORTS

Case 1 R R E was a 33-year-old white veteran, paraplegic at T-6 level, due to an automobile accident on January 12, 1953 A laminectomy of T-4,5,6 was performed on the day of the accident, no improvement resulted Re-exploration in July 1953 was followed by descent of the sensory level from T-4 to T-7 bilaterally, with dysesthesia of T-7 to T-9 dermatomes

The patient complained of severe girdle pains in his lower thorax and upper abdomen Repeated paravertebral blocks of T-6 to T-9 failed to affect the pain A bilateral posterior rhizotomy was performed on March 10, 1954 at T-5 to T-8, as well as a bilateral anterior rhizotomy at T-6 The patient stated that he had obtained no relief of his girdle pains

On April 23, 1956, he re-entered the hospital complaining of pain and spasticity of the upper abdominal muscles which were severe enough to interfere with his appetite Examination revealed intermittent board-like spasticity of the upper abdominal muscles Cystometry revealed a small bladder with a high intracystic pressure A bilateral rhizotomy of T-7, T-8, T-10 and T-11, sparing T-9, was recommended, but the patient refused to accept surgery Zoxazolamine treatment was therefore tried in an attempt to relieve his spasticity

On May 2, 1956 cystometric studies prior to flexin therapy showed an intracystic pressure of 47 cm of H_2O when the bladder was filled with 75 cc At this point severe upper abdominal muscle spasticity appeared At 100 cc of filling leakage occurred around the catheter See figure 1

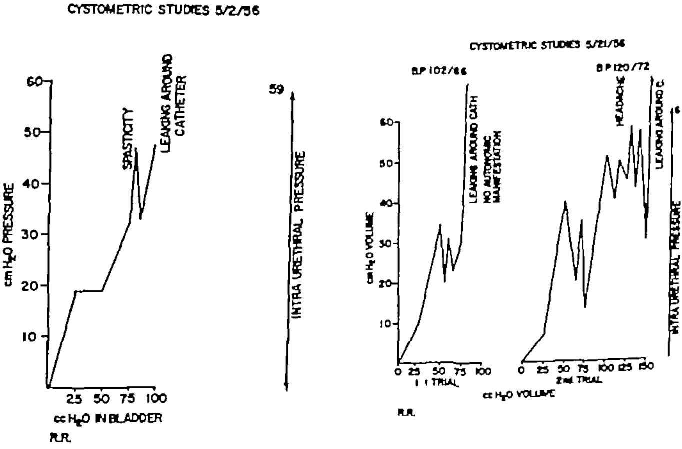


FIG 1

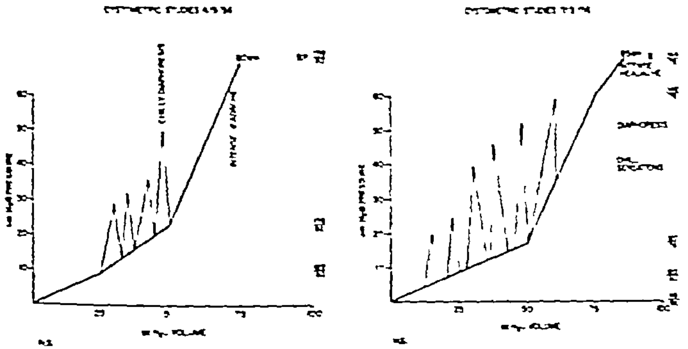


FIG 5

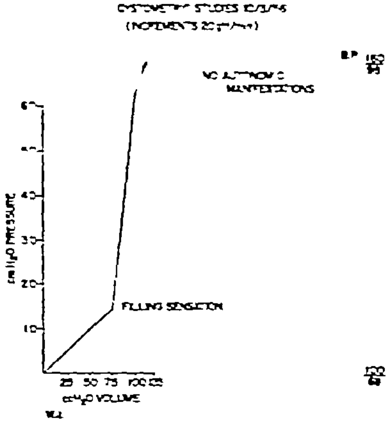


FIG 6

750 mg q i d was administered for one week The patient complained of mental symptoms on the higher dosage

Case 4 B R W , a 23-year-old quadriplegic had a cord lesion at C-5 level due to a diving accident on April 20 1953 Because of severe spasticity of the lower extremities bilateral obturator neurectomies femoral nerve crush, and a neurectomy of the motor branches of the right sciatic nerve were carried out in 1955 The patient continued to complain of severe spasticity of his upper extremities and of his abdominal muscles

Flexin therapy in dosage of 500 mg q i d was administered April 13 1956 to May 18, 1956, and from May 26 1956 to June 12, 1956 June 22, 1956 to July 14 1956 and from August 3 1956 to September 8 1956

The patient obtained no relief of the spasticity of the abdominal muscles nor of the upper extremities

Cystometry on April 9 1956 showed wide swings of intracystic pressure during the first 25 cc of filling with leakage around the catheter The patient had intense headaches clammy diaphoresis and blood pressure of 170/90 at 40 cc of filling See figure 4 Another examination on July 5 1956 again showed wide swings of intracystic pressure during the first 10 to 15 cc of filling with voiding at 20 cc of

Comment Neither subjective nor objective improvement occurred in the spasticity of the lower extremities or of the bladder in spite of zoxazolamine therapy for three weeks

Case 3 B J F was a 20-year-old white man, paraplegic, with a level of T 9 as a result of an automobile accident on August 22, 1955

The patient had severe spasticity of the lower extremities and the bladder He was treated by zoxazolamine 500 mg q i d from July 5, 1956 to August 14, 1956

Cystometric examination on July 3, 1956 showed a sharp rise in the intracystic pressure when the bladder was distended to 40 cc The pressure rose to over 80 cm of H_2O and leakage occurred around the catheter at 60 cc of fill Marked spasticity was evoked in the lower extremities See figure 3

On October 3, 1956 to October 9, 1956 he was treated with 750 mg flexin q i d The patient complained of "feeling high", but there was neither subjective nor objective evidence of any lessening of the spasticity of the lower extremities

Cystometry on October 10, 1956 again revealed a small, hypertonic bladder with sharp rise in the intracystic pressure and a total capacity of 60 cc See figure 3

Comment Neither subjective nor objective evidence indicated relief of spasticity of the lower extremities or of the bladder on flexin therapy at a dosage of 500 mg q i d for more than a month A similar lack of effect resulted when

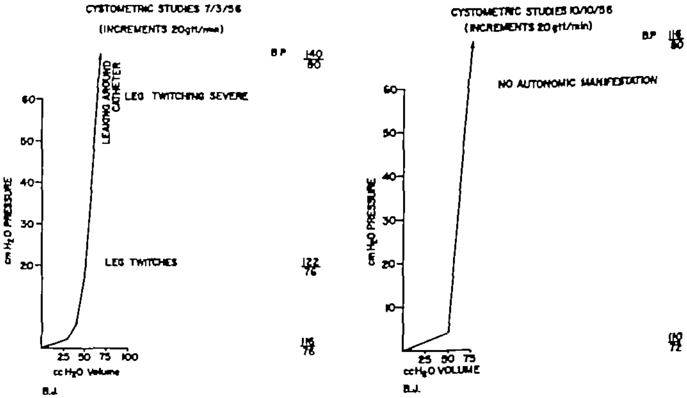


FIG 3

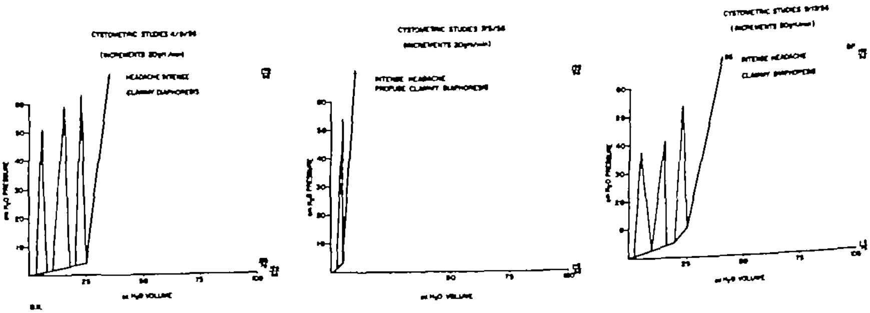


FIG 4

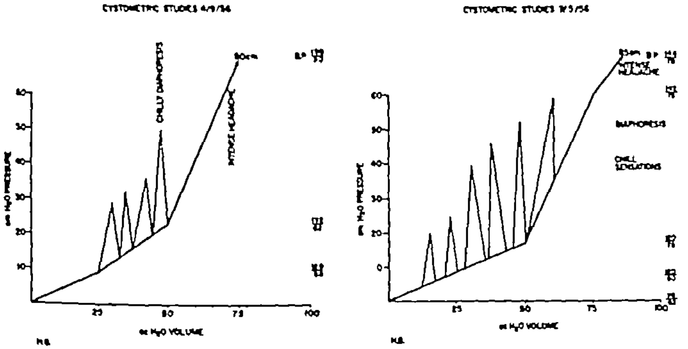
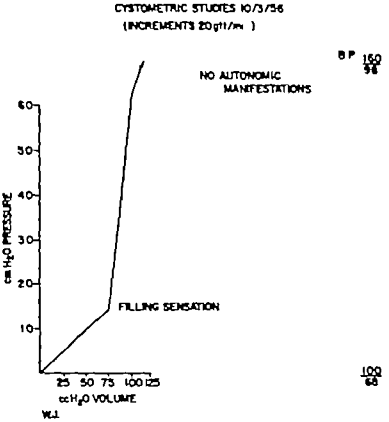


FIG 5



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The patient obtained no relief of the spasticity of the abdominal muscles nor of the upper extremities

Cystometry on April 9, 1956 showed wide swings of intracystic pressure during the first 25 cc of filling, with leakage around the catheter The patient had intense headaches, clammy diaphoresis and blood pressure of 170/90 at 40 cc of filling See figure 4 Another examination on July 5, 1956 again showed wide swings of intracystic pressure during the first 10 to 15 cc of filling, with voiding at 20 cc of capacity The patient had intense headache, profuse diaphoresis and blood pressure of 158/90 at that point See figure 4 On September 17, 1956 cystometry was characterized by wide swings of intracystic pressure during the first 25 cc of filling The patient voided at 40 cc He also experienced severe autonomic manifestations The blood pressure rose to 158/90 See figure 4

Case 5 H G F , a 23-year-old patient, became a quadriplegic as a result of an automobile accident on December 24, 1954 The spinal cord level of the injury was at C-7 This patient experienced severe spasticity which did not respond to a trial of equanil therapy On April 12, 1956 the patient was treated with zoxazolamine 500 mg q i d which was continued to April 19, 1956, the same therapy was again instituted from June 22, 1956 to June 29, 1956 No subjective improvement followed and no objective evidence of lessening of the over-all spasticity

Cystometry on April 9, 1956 showed a sharp rise in the intracystic pressure with wide swings between 25 and 50 cc of filling See figure 5 The patient voided at 75 cc At this point he had an intense headache, diaphoresis and experienced chilly sensations The blood pressure rose to 150/90 Another cystometric examination on July 5, 1956 showed practically identical results with severe headaches, diaphoresis, chilly sensations and voiding at 75 cc of filling See figure 5 The blood pressure was 144/78

Case 6 W J R was a 23-year-old incomplete quadriplegic as a result of an automobile accident on April 24, 1953 with fracture of C-5 vertebra The patient had severe spasticity of his bladder and of his lower extremities Rhizotomy was not advised because the patient had return of cutaneous sensation down to his toes, and because of the presence of sex function Flexin therapy was started on September 17, 1956 with a dosage of 500 mg q i d The dose was increased on October 3, 1956 to 750 mg q i d , and maintained at this level until October 10, 1956 On the larger dosage he complained of weakness and lightheadedness, but his bladder did not feel so irritable No improvement resulted in the spasticity of the lower extremities

Cystometric examination on October 3, 1956 showed a fairly sharp rise of the intracystic pressure up to 75 cc of filling The patient experienced a voiding sensation at this point Further filling of the bladder to 100 cc produced a sharp increase in the intracystic pressure The patient voided at 115 cc of filling See figure 6 The blood pressure rose to 160/98

SUMMARY AND CONCLUSIONS

Zoxazolamine (flexin) was administered to three paraplegic and three quadriplegic patients in a dosage of 500 mg q i d without lessening the spasticity of the skeletal muscles, as observed clinically

Cystometric examinations revealed no changes in the hypertonic bladders after flexin therapy

An increase of the dosage to 750 mg q i d failed to affect spasticity, but the patients complained of lightheadedness and one experienced weakness No other toxic effects were noted

Previous reports of effectiveness of this drug in the treatment of spasticity ld not be confirmed

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PHEOCHROMOCYTOMA: REPORT OF FIVE CASES, ONE A SPONTANEOUS CURE

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Much has been written in recent years about pheochromocytoma. Kvale and colleagues[1] in 1954 reported a personal series of 25 cases and Cahill,[2] in 1953, reviewed 139 cases, making it appear that this is a lesion worthy of consideration even though it is not commonly found in small centers. When to consider the possibility of this diagnosis is well explained by Pratt,[3] whose thoughts could be interpreted to imply that the diagnosis needs to be considered in almost any case of hypertension. The clinical impression can be confirmed with the help of adrenergic blocking agents such as regitine, provocative agents, of which histamine is at present the most widely used, x-rays including retroperitoneal pneumograms, and biochemical tests for increased amounts of adrenalin and noradrenalin in the urine and blood. The biochemical tests which have been described by Von Euler[4] and Goldenberg and associates[5] were not locally available during this study. In the present study another test mentioned in a previous report,[6] was used, namely, the injection of patients' urine into dogs for detection of pressor substances.

During the past 4 years 5 cases of pheochromocytoma have been confirmed by this method (a dog bioassay test) and proved by surgery. During this time urine from more than 150 patients suspected of having pheochromocytoma has been tested by this method. Seven patients with negative responses to this test, but clinically positive responses to regitine, have been found on followup study not to have pheochromocytoma. Three of these were explored, with negative findings. Retroperitoneal pneumograms have given valuable aid in localizing the tumors in the 4 cases in which the method was employed. Retroperitoneal pneumograms have given no false positive results. This small series is being reported not only because some of the cases are unusual, but also because it is of some interest that prior to 1952, when the first case was found, a clinical diagnosis of pheochromocytoma had not been made and proved in this city.

Read at annual meeting of South Central Section of American Urological Association, Mexico City, October 28–November 1, 1956.

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CASE REPORTS

Case 1. A 14-year-old white boy, the subject of a previous report,[6] was admitted to the University Hospital in December 1952. He gave a history of occipital headaches of 4 months' duration, nausea and projectile vomiting of 2 months' duration, and a 19½ pound weight loss. He had hypertensive retinopathy, with a blood pressure of 195/155. No masses were felt in the abdomen, and vigorous palpation failed to influence the blood pressure. Routine laboratory tests were not remarkable. The excretory urogram was normal. Retroperitoneal pneumography, using oxygen, outlined a soft tissue mass medial to the right kidney, measuring 8 by 6 cm. The injection of benzodioxane produced a blood pressure drop to 110/60 from 230/160. Pressor substances were found in the patient's urine by recording a rise in blood pressure in a dog following injection of the urine.

At surgery, a 108.4 gm. tumor was removed. This tumor was found between the aorta and the vena cava, just medial to the right kidney. The patient required noradrenalin for 48 hours to sustain his blood pressure following surgery. On the fourth day a staphylococcal septicemia developed. The abdomen was subsequently explored, but no abscess was found. The patient died 22 days after the original surgery. The pathology report on the tumor revealed a benign pheochromocytoma. This tumor was found to contain norepinephrine. No autopsy was obtained.

Case 2 (spontaneous cure). The patient, a 66-year-old, moderately obese white woman was admitted to Wesley Hospital on January 30, 1954, in a state of shock with acute pain in the abdomen. She had been followed as an outpatient for several weeks because of bouts of hypertension to 260/170, with her normal pressure usually being 120/70. She had frequent headaches and some vague complaints consisting of choking sensations at night and tachycardia. She had known gallbladder disease, which caused attacks of pain, nausea, and vomiting. Regitine, 5 mg. intramuscularly, had produced a blood pressure drop from 140/90 to 90/50 and on other occasions from 250/120 to 180/90. The patient's urine was found positive for pressor substances by a dog bioassay test (fig. 1, *A*). Two days before admission an acute illness developed rather rapidly. This attack consisted primarily of pain and tenderness in the right upper abdominal quadrant and was thought to be a gallbladder attack. Her blood pressure remained over 180/90 from this time on. On this admission her blood pressure was 240/120 and she appeared acutely ill, with rapid pulse and rigidity in the right upper quadrant of the abdomen. Her eyegrounds were normal, her blood counts were within normal limits, and a routine urinalysis showed 2 plus albuminuria but was otherwise negative.

It was deemed necessary to explore the patient's abdomen, since the clinical impression was that she probably had a ruptured gallbladder. At exploration, her blood pressure dropped to a normal range and remained there. There was a moderate amount of serosanguineous fluid in the abdomen, as well as a large (football size) hemorrhagic mass in the right retroperitoneal space. Gallstones were palpated but otherwise the intra-abdominal contents were negative Her condition made further surgery inadvisable and the abdomen was closed On return to her room following surgery her blood pressure rose to 196 100 and 5 mg of regitine was given which seemed to control her blood pressure well It remained fairly steady except for small fluctuations thereafter The rectal temperature rose to 103F in the first 24 hours and it fell to normal on the third postoperative day

Urine collected on the fifth postoperative day showed no pressor substances by the dog bioassay test (fig 1 *B*) although her blood pressure had reached 154 68 on that particular day By this time x-rays were possible and an excretory

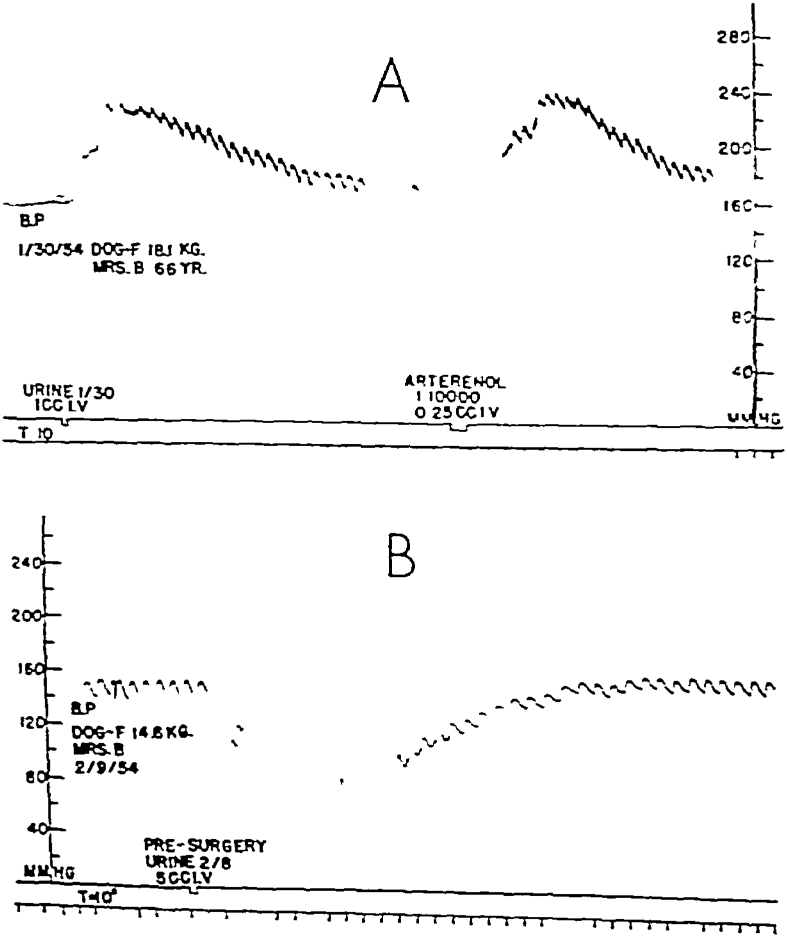

FIG 1 Case 2 A, tracing of dog bioassay test on urine shows positive response and a positive control using arterenol *B* tracing of dog bioassay test on urine collected 4 days before surgery on adrenal tumor shows negative response

CASE REPORTS

Case 1 A 14-year-old white boy, the subject of a previous report,[6] was admitted to the University Hospital in December 1952 He gave a history of occipital headaches of 4 months' duration, nausea and projectile vomiting of 2 months' duration, and a 19½ pound weight loss He had hypertensive retinopathy, with a blood pressure of 195/155 No masses were felt in the abdomen, and vigorous palpation failed to influence the blood pressure Routine laboratory tests were not remarkable The excretory urogram was normal Retroperitoneal pneumography, using oxygen, outlined a soft tissue mass medial to the right kidney, measuring 8 by 6 cm The injection of benzodioxane produced a blood pressure drop to 110/60 from 230/160 Pressor substances were found in the patient's urine by recording a rise in blood pressure in a dog following injection of the urine

At surgery, a 108 4 gm tumor was removed This tumor was found between the aorta and the vena cava, just medial to the right kidney The patient required noradrenalin for 48 hours to sustain his blood pressure following surgery On the fourth day a staphylococcal septicemia developed The abdomen was subsequently explored, but no abscess was found The patient died 22 days after the original surgery The pathology report on the tumor revealed a benign pheochromocytoma This tumor was found to contain norepinephrine No autopsy was obtained

Case 2 (*spontaneous cure*) The patient, a 66-year-old, moderately obese white woman was admitted to Wesley Hospital on January 30, 1954, in a state of shock with acute pain in the abdomen She had been followed as an outpatient for several weeks because of bouts of hypertension to 260/170, with her normal pressure usually being 120/70 She had frequent headaches and some vague complaints consisting of choking sensations at night and tachycardia She had known gallbladder disease, which caused attacks of pain, nausea, and vomiting Regitine, 5 mg intramuscularly, had produced a blood pressure drop from 140/90 to 90/50 and on other occasions from 250/120 to 180/90 The patient's urine was found positive for pressor substances by a dog bioassay test (fig 1, *A*) Two days before admission an acute illness developed rather rapidly This attack consisted primarily of pain and tenderness in the right upper abdominal quadrant and was thought to be a gallbladder attack Her blood pressure remained over 180/90 from this time on On this admission her blood pressure was 240/120 and she appeared acutely ill, with rapid pulse and rigidity in the right upper quadrant of the abdomen Her eyegrounds were normal, her blood counts were within normal limits, and a routine urinalysis showed 2 plus albuminuria but was otherwise negative

It was deemed necessary to explore the patient's abdomen, since the clinical impression was that she probably had a ruptured gallbladder At exploration, her blood pressure dropped to a normal range and remained there There was a moderate amount of serosanguineous fluid in the abdomen, as well as a large (football size) hemorrhagic mass in the right retroperitoneal space Gallstones were palpated but otherwise the intra-abdominal contents were negative. Her condition made further surgery inadvisable and the abdomen was closed. On return to her room following surgery her blood pressure rose to 196/100 and 5 mg. of regitine was given which seemed to control her blood pressure well. It remained fairly steady except for small fluctuations thereafter. The rectal temperature rose to 103F in the first 24 hours and it fell to normal on the third postoperative day.

Urine collected on the fifth postoperative day showed no pressor substances by the dog bioassay test (fig. 1 *B*) although her blood pressure had reached 154/68 on that particular day. By this time x-rays were possible and an excretory

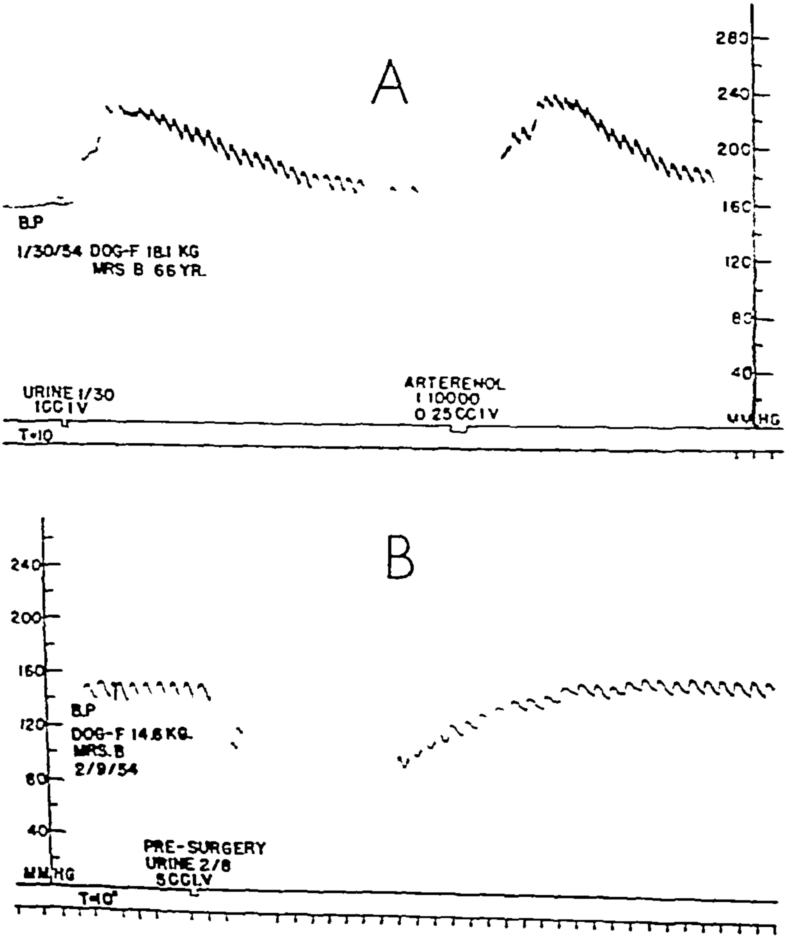

FIG. 1. Case 2. *A*, tracing of dog bioassay test on urine shows positive response, and a positive control using arterenol. *B*, tracing of dog bioassay test on urine collected 4 days before surgery on adrenal tumor shows negative response.

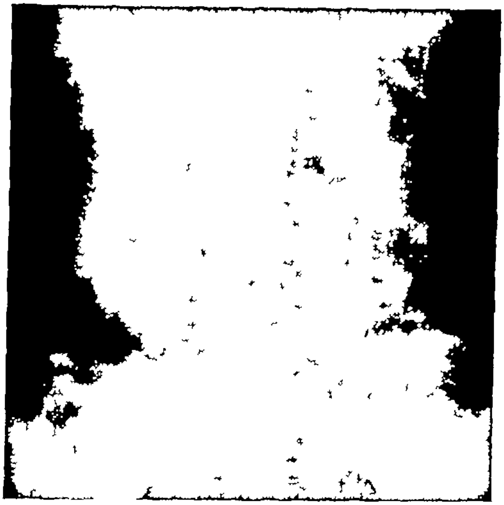

FIG 2 Case 2 Excretory urogram, made after the abdominal exploration, shows mass above right kidney

urogram showed a mass above the right kidney (fig 2) On February 8 nine days after the original operation, she was explored again through a right thoracoabdominal incision and a large hemorrhagic mass in the region of the right adrenal gland was found Fragments of tumor and clot were removed The adrenal gland was not identified but a large vein, thought to have been the central vein of the adrenal, was found and ligated During the procedure the blood pressure rose on one occasion to 170 systolic, but no adrenolytic agent was used and it dropped immediately Her course was uneventful

Pathologic study revealed much necrotic tissue with one section showing normal adrenal and adjacent pheochromocytoma, probably benign Repeat urine studies, by dog injections, have remained negative for pressor substances and there have been no findings of metastasis The patient has remained well for 32 months since her surgery

Comment It is felt, in retrospect, that this patient destroyed the pheochromocytoma by a spontaneous hemorrhage This appears to be the first such case reported in the literature A case[7] has been reported in which rupture of the tumor occurred at the time of surgery

Case 3 (malignant ectopic pheochromocytoma) A 48-year-old white man was admitted to Wesley Hospital on April 19, 1954 He gave a history of fatigue, constipation, and frontal headache which had occurred, especially on arising, for the past two or three months He had noted excessive perspiration for 2 years and decreasing tolerance to hot weather Physical examination revealed a well developed and well nourished man, not acutely ill His blood pressure was 116/70 and eyegrounds were normal There were some reflex changes from an old luetic infection He had a questionable mass in the region of the umbilicus on the right side Routine laboratory studies were within normal limits, except

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[7] Middleton, A W *Pheochromocytoma A case report presenting unusual clinical features and successful surgical removal* J Urol **63** 446–450, 1950

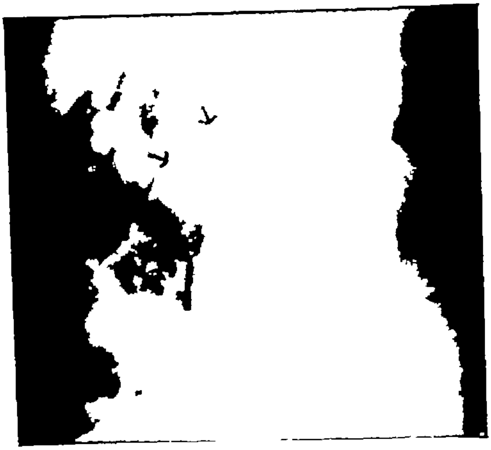

FIG 3 Case 3 Presacral oxygen study shows mass between spine and lower right kidney

for a positive serology His basal metabolism rate was 40 plus and he had a diabetic type glucose tolerance curve An excretory urogram was normal except for some faint, unidentified calcification just to the right of the interspace between L-2 and L-3 The chest x-ray was normal Retroperitoneal pneumograms revealed a soft tissue mass to the right of the midportion (fig 3) of the lumbar spine, extending from the upper border of the body of L-3 to the lower border of L-4 Flecks of calcium were seen in its lower portion A blood pressure rise was noticed on palpation of this tumor from 116/70 to 180/110 It seemed to be sustained at that level, but dropped to 150/90 with the administration of 5 mg of regitine Urine studies for pressor substances by dog injection were positive

Surgical exploration through a transverse abdominal incision was carried out, with the removal of a 5 cm tumor weighing 153 gm Removal of the right kidney was necessary because the vessels of the pedicle of the right kidney were surrounded by this tumor The tumor extended into the vena cava, apparently through a small communicating vessel in a mushroom fashion, with a tumor nodule in the vena cava measuring 2 5 cm in diameter This required removal of a piece of the wall of the vena cava, to which this tumor was firmly adherent Pathologic study confirmed this to be a malignant pheochromocytoma and pressor substances were found in the tumor extract The patient's course was stormy but he recovered completely and has no evidence of metastasis 2½ years following surgery Urine studies for pressor substances have continued to be negative

Two months after this paper was read, the patient was found to have some elevation of his blood pressure and the mass in the abdomen The urine was found positive again for pressor substances by dog injection Abdominal exploration confirmed the clinical impression of recurrent pheochromocytoma The patient also had some adenopathy in the left supraclavicular region and a biopsy of a node was found positive for pheochromocytoma The patient was given two thousand roentgens of x-ray to each of four abdominal portals and three thousand

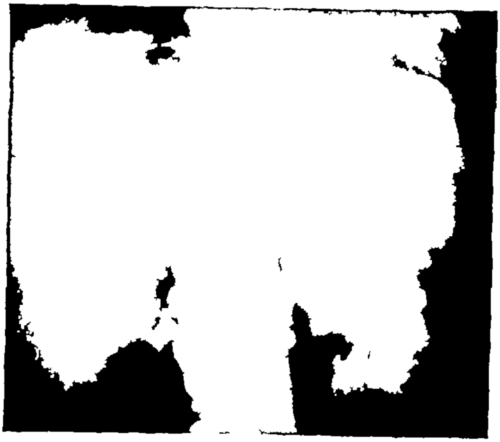

FIG 4 Case 4 Pre sacral oxygen study shows bilateral adrenal tumors

roentgens to the left cervical region Some clinical improvement resulted, and on May 21, 1957, a chest x-ray was negative

Case 4 (*multiple bilateral pheochromocytoma*) A 39-year-old, healthy-appearing white man was admitted to Wesley Hospital on July 9, 1955, for evaluation of total gross hematuria of 2 days' duration, associated with urgency of urination

He complained of an intolerance to heat of 2 years' duration and intermittent severe headaches of 1 year's duration He felt extremely nervous and jittery with these headaches Physical examination revealed blood pressure of 200/120 and a loud systolic murmur, best heard over the pulmonic area His eyegrounds were negative Laboratory studies revealed a normal hemogram Routine urine studies showed 2 plus albuminuria, 4 plus sugar, and a few red blood cells in the microscopic examination He had a diabetic type glucose tolerance curve X-rays, including chest film and excretory urogram, were negative except for slight rotation of the left kidney Retroperitoneal pneumograms (fig 4) outlined bilateral adrenal tumors Cystoscopy was negative except for a ureterocele on the left, which was thought to be the source of the hematuria Regitine, 5 mg intramuscularly, produced a drop in blood pressure from 180/120 to 110/70 The dog bioassay tests for pressor substances in the urine were positive

Surgery was performed through a transverse upper abdominal incision Exposure was difficult because of the high position of these tumors on each side and the incision had to be extended, entering both pleural cavities During the period of opening the abdomen and removing the right adrenal tumor, the blood pressure could not be kept below 260/130, even though during this period of 1 hour and 30 minutes 67 5 mg of regitine and 14 mg of benzodioxane were given The pressure dropped to 150/90 with removal of the right tumor and fluctuated, but not in dangerous levels, while a tumor on the left side was removed Following this, the blood pressure rose to 200/130 again Further search was made and another tumor was found projecting posteriorly to the superior pole of the left kidney Following the difficult removal of this third tumor, the patient's blood pressure fell to levels which could not be recorded He was sustained immediately with noradrenalin and the wound was closed His blood pressure became difficult to maintain, even with intravenous noradrenalin, and the patient died on the following morning, 20 hours after he had returned from surgery The patient had been given cortisone, 200 mg daily (orally), for 2 days prior to surgery and he was given 200 mg intramuscularly during the day of surgery

Pathologic study of the tumors revealed that adrenal tissue had been incorporated in all three tumors It was speculated that all of the adrenal tissue had been removed The tumors weighed 100 gm , 49 gm , and 71 gm The microscopic diagnosis of each was benign pheochromocytoma

Autopsy revealed no remaining tumor or adrenal tissue There was no significant hemorrhage in the operative area Rather severe pulmonary edema, moderate hydrothorax, and hydroperitoneum were present, and all tissue studied was edematous The heart showed typical hypertensive type hypertrophy and there was minimal atherosclerotic change

Comment The only additional therapy that might have changed the course of this patient's illness would have been massive doses of intravenous hydrocortisone sodium succinate Even though he seemed to have enough cortisone to compensate for total adrenalectomy, it did not compensate for the tremendous stress produced by the major surgical procedure

Case 5 A 32-year-old, healthy-appearing white man was admitted to Wesley Hospital on February 23, 1956, complaining of severe headaches of several months' duration They started in the left occipital region and radiated all over the head They were preceded by a peculiar thrill sensation The headaches were getting more frequent and the patient looked actually wild during the episodes They were found to be associated with a blood pressure rise and palpitations Physical examination was essentially negative The blood pressure was 140/90 Laboratory tests, including routine urine and blood studies, were

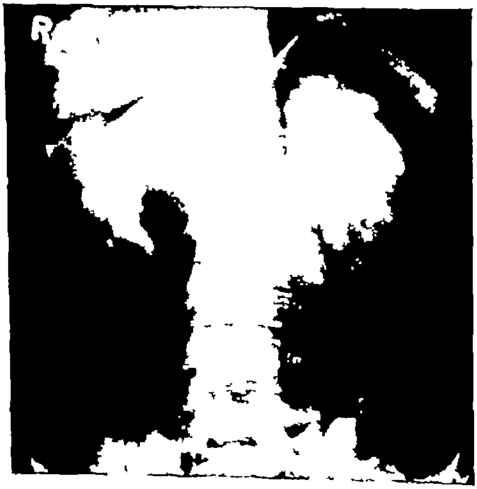

FIG 5 Presacral oxygen and excretory urogram shows mass in right adrenal area

negative The glucose tolerance curve was normal A chest x-ray and an excretory urogram were negative Retroperitoneal pneumograms (fig 5) revealed a mass in the region of the right adrenal gland During a severe headache, with the blood pressure remaining at 220/100, 5 mg of regitine intramuscularly produced a drop to 170/80 Dog bioassay tests for pressor substances in the patient's urine were positive

Surgery was performed through a transverse abdominal incision The blood pressure rose to 280 systolic on opening of the abdomen, but it decreased to safe levels with 5 mg of regitine During the procedure, regitine was given only on two other occasions, when the blood pressure rose to 290 systolic The patient was easily controlled with noradrenalin when the tumor was removed and his blood pressure remained at normal levels His course was uneventful, with the use of noradrenalin no longer needed after the second postoperative day The pathology report indicated benign pheochromocytoma containing large amounts of pressor substances

SUMMARY AND CONCLUSIONS

Four cases of pheochromocytoma have been added to the literature One seemed definitely malignant and the other three were histologically benign A fifth case, which had been reported previously, is reviewed

One of these cases (case 2) represents a spontaneous cure by hemorrhage into the tumor, as demonstrated by disappearance of pressor substances from the urine before definitive surgery was performed

Provocative tests were not used in this series, but benzodioxane and regitine were very helpful The intravenous injection of patients' urine into dogs to demonstrate pressor substances was positive in each case and retroperitoneal pneumograms localized the tumor or tumors in each case in which it was used

The finding of 5 cases with pheochromocytoma in the past 4 years, and in a community where none had previously been reported, suggests the value of all the publicity given this tumor in recent years

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A RECURRENT NONFUNCTIONING TUMOR OF THE ADRENAL CAPSULE CASE REPORT

RICARDO ANGULO

As pointed out by Cahill benign tumors of the adrenal cortex grow silently until they reach great size The case presented is an example of such growth and is especially interesting because we were able to follow recurrence of the tumor after one operation and operate upon the patient the second time successfully

CASE REPORT

Mrs L S 45 years of age white married had borne three children When she was first seen December 17 1947 she stated that for several months she had been suffering with pain in the left flank radiating to the pelvic crest in that side She had also noticed considerable swelling in the left abdomino-lumbar region which was visually evident She had lost a few pounds and lacked appetite She had not had any urinary difficulties and had not observed any gross hormonal disturbances

By palpation a tumor was outlined extending from beneath the left costal margin to the pelvic crest and to the midline of the abdomen The tumor was fairly movable especially laterally Movement produced pain Percussion indicated that the mass was solid and that the intestines were not anteriorly superimposed The surface was smooth

Additional history elicited was as follows October 5 1945 the patient had suffered with intestinal intoxication following which pain in the region of the gallbladder developed and also jaundice of the skin and conjunctivae

X-ray examination of the gastrointestinal tract including barium enema was reported as showing Delay in passage through the cecum and lower portion of the ascending colon diminished filling of the entire descending colon especially in the lower third but that region is freely movable by external manipulation The splenic flexure is markedly displaced downwards to the left iliac fossa as is also the transverse colon which is seen at the level of the inferior pelvic outlet when the patient is standing

December 24 1947 a radiogram of the gallbladder was reported Fifteen hours after ingestion of the dye the concentration in the gallbladder is so slight as to preclude visualization of the morphologic characteristics except those of position and size which are apparently within normal limits Diagnosis pathologic gallbladder

December 27 1947 an excretory urogram revealed ptosis of the right kidney with its lower pole near the iliac crest good excretion of dye some increase of the size of the kidney on the left excellent excretion of the dye The left kidney is seen in the iliac fossa The calyces are impinged by a tumor which reaches to the level of the first lumbar vertebra (fig 1 A) These findings are indicative of a tumor in the region of the left kidney The urinary bladder is normal

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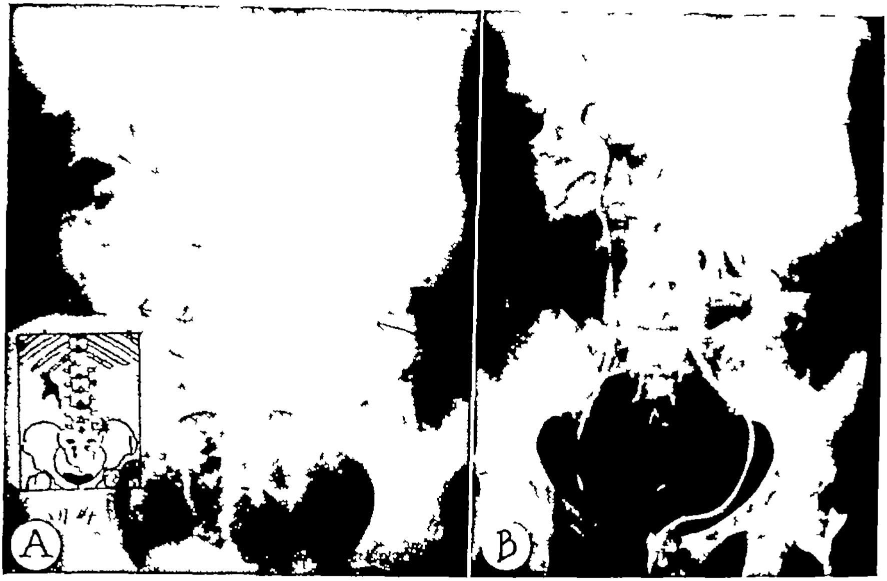

FIG 1

At cystoscopic examinations on January 10, 1948 catheters were easily passed up each ureter The urinary concentration of the two sides was equal and the findings in the sediment were not significant The anatomical findings in the renal pelves are shown in fig 1, *B*

Following other indicated examinations, operation was accomplished January 13, 1948 with the patient under general anesthesia The diagnosis was left retroperitoneal tumor A left lumbar incision was made and extended forward by section of the oblique abdominal muscles The tumor was found lying above the kidney In freeing the tumor numerous peripheral vessels of fair size were ligated without difficulty On the medial aspect firm adhesions were found to the peritoneum, which was opened and closed with fine catgut After the tumor was removed, the left kidney was fixed by the technique of Surraco The wound was closed in layers A small cigarette drain was left in the wound four days The postoperative course was uneventful The skin sutures were removed on the eighth day and the patient was discharged the fourteenth day

The pathologist, Dr Urteaga, reported "The resected tumor weighs 1875 gm Its longest diameter is 18 cm (fig 2), the consistency is soft, the color yellowish-pink There is a fibrous, vascular capsule Transection reveals a homogeneous cortex of 2 to 3 cm in thickness The central portion shows foci of hemorrhage and necrosis with fibrous bands The microscopic sections are those of a cortical adenoma" (fig 3)

When seen 2 years later, the patient had gained 10 kilograms and was living normally She was next seen August 12, 1955 because of recurrence of the original symptoms, rapid loss of weight, lack of appetite and pain in the left lumbar region radiating to the flank and left abdomen She had noted recurrence of a tumor with visible swelling in the left flank to approximately the same degree as that

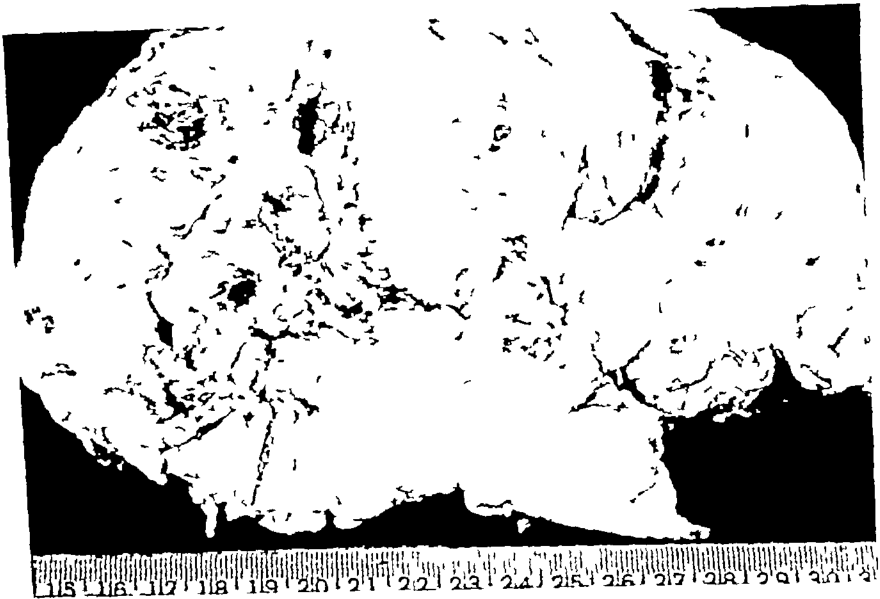

FIG 2

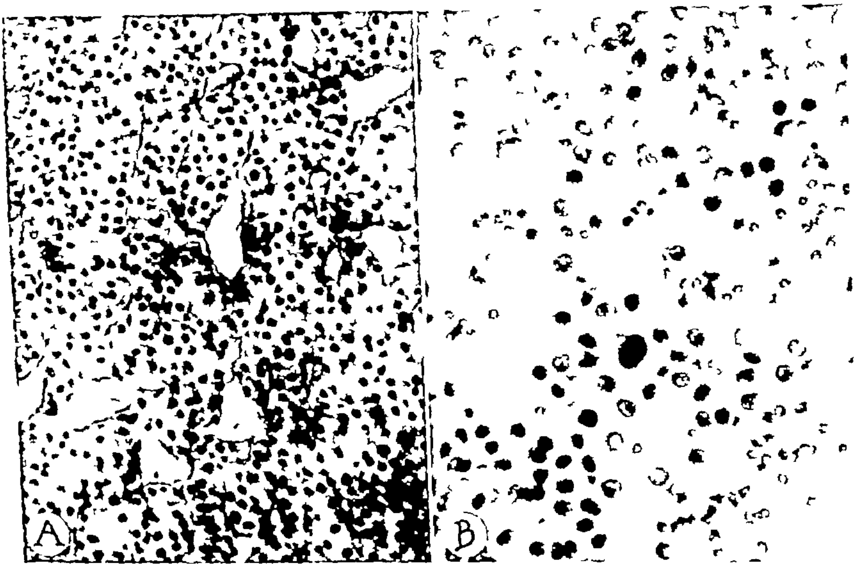

FIG 3

produced by the original tumor On palpation the tumor was freely movable laterally and medially and was apparently not adherent to the surrounding tissues There was no evidence of endocrine disturbances The blood pressure was within normal limits as was the blood count Other examinations disclosed no significant abnormalities The diagnosis was recurrent tumor of the left suprarenal capsule

Operation under spinal anesthesia was performed September 7 The scar of the previous operation was excised, and the muscular layers were divided to reach the renal fossa The left kidney was found in the upper part of the incision below the twelfth rib (fig 4) Beneath it lay the tumor surrounded by numerous blood vessels which were easily ligated In attempting to free the tumor an-

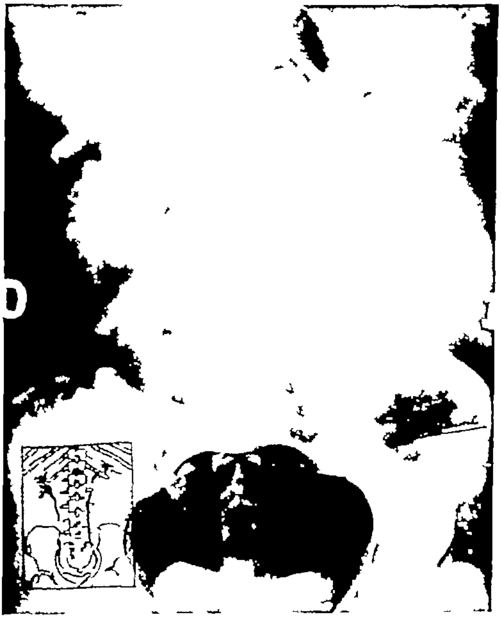

FIG 4

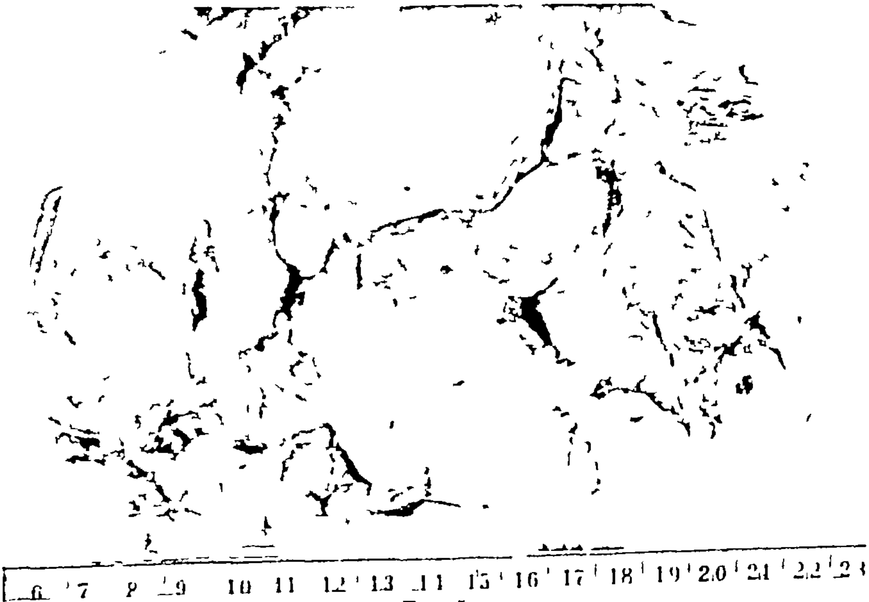

FIG 5

teriorly, dense adhesions between the parietal peritoneum and the descending colon were encountered The peritoneum was then opened the tumor freed and the peritoneum carefully closed with fine catgut In freeing the tumor the fibrous capsule was torn The wound was debrided and closed by mass suture of the muscular layers with a cigarette drain which was left in place five days

During the first three postoperative days the patient had a temperature of 38C and vomited bile-stained material Thereafter her course was uneventful She left the hospital on the sixteenth day

Dr Urteaga reported A suprarenal tumor of 1000 gm (fig 5) oval in shape with a major diameter of 16 cm The consistency is soft The color is brown-yellow It is surrounded by a fibrous capsule which was apparently torn during the operative manipulation This tumor is more friable than the original one but the cut section is similar Teased tissue examined by the method of Papanicolaou shows groups of typical cortical tumor cells without evidence of malignancy Microscopic study of stained sections shows proliferation of benign cortical cells which have the glomerulo-fascicular appearance of suprarenal gland There is no evidence of malignancy Diagnosis Cortical adenoma Comparison with sections of the original tumor reveal exact similarity (See figure 3)

When seen August 15 1956 the patient was in excellent health and had gained 8 kilograms

Jiron Arica 882 Lima Peru

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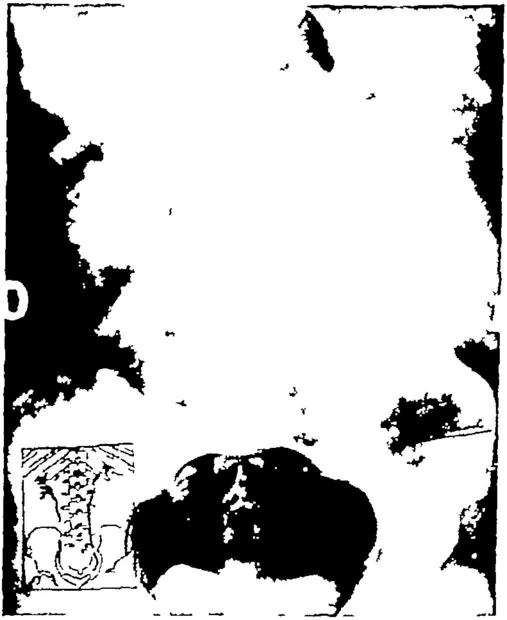
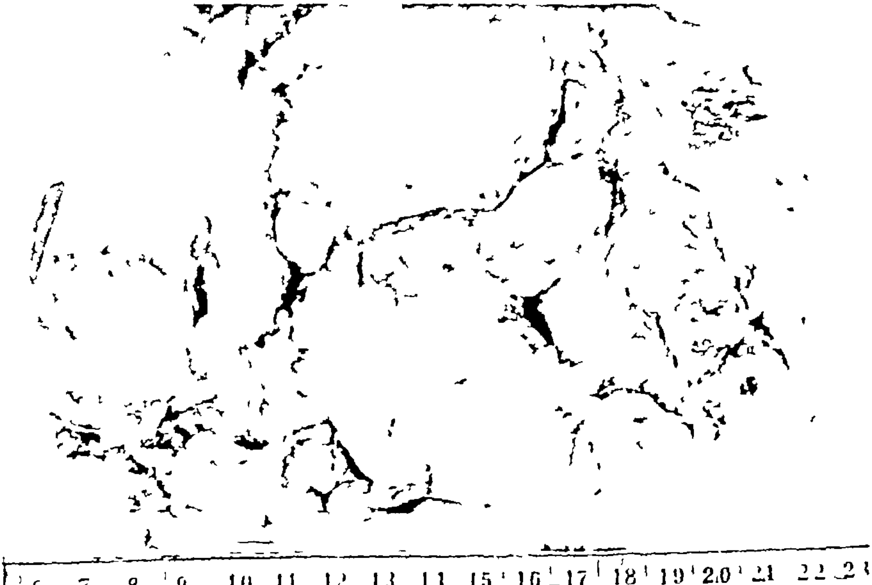


Fig 4



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URIC ACID CALCULI

RUSSELL E. ALLYN

The paucity of articles in current literature regarding uric acid calculi bears no relationship to their occurrence in the practice of urology. Only 5 reports since 1950 are listed in the accumulated index, three that were reviewed were of a technical nature, the other two were unobtainable. Likewise, since 1950, in the Yearbook of Urology, only one article is reviewed, and that regarding their occurrence in cases of previously proven gout. Scrutiny of five late textbooks of urology discloses that only one devotes more than a paragraph of three sentences to this interesting and often perplexing subject. It is merely reiterated from text to text that uric acid calculi comprise between 4 per cent and 10 per cent of all renal calculi, are yellow in color, smooth and ovoid in shape, pass with little pain, and do not cast a shadow on an x-ray film.

It is the author's opinion that uric acid calculi are more common than previously supposed and their diagnosis easy when suspicion is aroused, and the treatment highly gratifying to both patient and physician.

Since this is purely a clinical report of our experiences in this intriguing subject, we shall divide our cases into four clinical groups, and present typical representative cases of each group.

Group 1 is perhaps the most common, the least diagnosed, the easiest treated and the least important. The criteria are: Recurrent, typical renal colic associated with the discovery, by cystoscopy, of golden yellow crystals, or gold sand, in the bladder, elevated blood uric acid content, a normal intravenous urogram and retrograde pyelogram, and complete relief of symptoms with the appropriate therapy.

A typical case is that of I. G., a white, *mildly diabetic man aged 64*, admitted to Harrisburg Hospital on September 12, 1956 on a private medical service with various complaints including recurrent renal colic. An intravenous urogram was within normal limits, and urological consultation was sought because of recurrent renal colic. Cystoscopy on September 22 disclosed many small uric acid crystals and calculi in the bladder. A retrograde pyelogram was normal. Blood uric acid determination at this time was 8.1 mg. per cent. A diagnosis of recurrent colic due to the passage of small uric acid calculi and crystals was made, the patient was placed upon a high fluid intake, sodium bicarbonate and benamid by mouth. The blood uric acid determination has fallen to within normal limits, and the symptoms have not recurred.

Group 2 is merely a progression of group 1, until plugging of the ureter with uric acid crystals and debris produces a nonfunctioning kidney that is disclosed by intravenous urography, and superimposed infection add chills and fever to complicate the picture.

A. L., a white man aged 34, was admitted *to a private medical service* of Harrisburg Hospital April 3, 1956 with chills, fever, abdominal pain, nausea, and

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Read at annual meeting of Mid-Atlantic Section, American Urological Association vomiting of 3 days' duration The diagnosis was intestinal obstruction A diagnosis of paralytic ileus, etiology undetermined, was made from a study of a gastrointestinal series and a barium enema The pain gradually became localized to the left flank and intravenous urography revealed a nonfunctioning left kidney, cause undetermined A cystoscopic examination on April 7 revealed thousands of small, golden yellow particles in the bladder Both ureters were catheterized with ease, and a large amount of dirty, foul urine obtained from the left kidney A catheter was left in place for drainage Blood uric acid determination at this time was 8 7 mg per cent Treatment consisted of forcing fluids, alkalization of urine with sodium bicarbonate and benamid by mouth The symptoms immediately subsided, and followup intravenous urograms revealed normal functioning upper urinary tracts with the possibility of polycystic kidney disease The symptoms have not recurred, and on therapy, the blood uric acid content has remained within normal limits

Group 3 is similar to the previous groups except that a definite calculus is present and produces a filling defect This calculus may pass spontaneously, or it may have to be removed surgically We shall present two typical cases

H P, a white man aged 47, was seen in the office on November 3, 1954 with the chief complaint of recurrent renal colic From 1930 until 1954 by actual count, the patient had passed more than 2,000 renal calculi, mostly from the left kidney, passing as many as 50 per month Grossly, these calculi had all the characteristics of pure uric acid calculi, and were so proven by chemical analysis Cystoscopy revealed a virtual snowstorm of golden sand within the bladder In addition, the patient was a mild diabetic The blood uric acid content at this time was 27 4 mg per cent He was referred to an internist with the diagnoses of recurrent renal calculi and diabetes mellitus Therapy consisted of diet, forcing fluids, sodium bicarbonate and benamid His blood uric acid determination has gradually fallen to 4 4 mg per cent, and the renal colic has not recurred

The second case is that of J C, a white man aged 37, who was admitted to the Harrisburg Hospital on September 24, 1956, with the chief complaints of hematuria and left flank pain Cystoscopy was within normal limits Urine collected from the left kidney was dirty and grossly bloody Intravenous urography and retrograde pyelography revealed a horseshoe kidney, left hydronephrosis and a filling defect within the left renal pelvis The blood uric acid determination was 7 8 mg per cent At operation, on October 2, division of the isthmus of the horseshoe kidney, left nephropexy, and left pelviolithotomy were accomplished Chemical analysis of the calculus revealed it to be composed of pure uric acid Postoperatively the patient was placed on forced fluids, sodium bicarbonate, and benamid His blood uric acid content is now 3 4 mg per cent and his symptoms have not recurred

Group 4 is exactly like group 3, except that the blood uric acid content is within normal limits In our experience, patients with pure uric acid calculi and normal blood uric acid content are perhaps more common than those with elevated blood uric acid determinations Again, we would like to present two typical cases

Mrs M G, a white woman aged 67, was seen in the office on January 23

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Since this is purely a clinical report of our experiences in this intriguing subject, we shall divide our cases into four clinical groups, and present typical representative cases of each group

Group 1 is perhaps the most common, the least diagnosed, the easiest treated and the least important The criteria are Recurrent, typical renal colic associated with the discovery, by cystoscopy, of golden yellow crystals, or gold sand, in the bladder, elevated blood uric acid content, a normal intravenous urogram and retrograde pyelogram, and complete relief of symptoms with the appropriate therapy

A typical case is that of I G , a white, mildly diabetic man aged 64, admitted to Harrisburg Hospital on September 12, 1956 on a private medical service with various complaints including recurrent renal colic An intravenous urogram was within normal limits, and urological consultation was sought because of recurrent renal colic Cystoscopy on September 22 disclosed many small uric acid crystals and calculi in the bladder A retrograde pyelogram was normal Blood uric acid determination at this time was 8 1 mg per cent A diagnosis of recurrent colic due to the passage of small uric acid calculi and crystals was made, the patient was placed upon a high fluid intake, sodium bicarbonate and benamid by mouth The blood uric acid determination has fallen to within normal limits, and the symptoms have not recurred

Group 2 is merely a progression of group 1, until plugging of the ureter with uric acid crystals and debris produces a nonfunctioning kidney that is disclosed by intravenous urography, and superimposed infection add chills and fever to complicate the picture

A L , a white man aged 34, was admitted to a private medical service of Harrisburg Hospital April 3, 1956 with chills, fever, abdominal pain, nausea, and

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Read at annual meeting of Mid Atlantic Section, American Urological Association Virginia Beach, Va March 21-24, 1957 vomiting of 3 days' duration The diagnosis was intestinal obstruction A diagnosis of paralytic ileus, etiology undetermined, was made from a study of a gastrointestinal series and a barium enema The pain gradually became localized to the left flank and intravenous urography revealed a nonfunctioning left kidney, cause undetermined A cystoscopic examination on April 7 revealed thousands of small, golden yellow particles in the bladder Both ureters were catheterized with ease, and a large amount of dirty, foul urine obtained from the left kidney A catheter was left in place for drainage Blood uric acid determination at this time was 8 7 mg per cent Treatment consisted of forcing fluids, alkalization of urine with sodium bicarbonate and benamid by mouth The symptoms immediately subsided, and followup intravenous urograms revealed normal functioning upper urinary tracts with the possibility of polycystic kidney disease The symptoms have not recurred, and on therapy, the blood uric acid content has remained within normal limits

Group 3 is similar to the previous groups except that a definite calculus is present and produces a filling defect This calculus may pass spontaneously, or it may have to be removed surgically We shall present two typical cases

H P, a white man aged 47, was seen in the office on November 3, 1954 with the chief complaint of recurrent renal colic From 1930 until 1954 by actual count, the patient had passed more than 2,000 renal calculi, mostly from the left kidney, passing as many as 50 per month Grossly, these calculi had all the characteristics of pure uric acid calculi, and were so proven by chemical analysis Cystoscopy revealed a virtual snowstorm of golden sand within the bladder In addition, the patient was a mild diabetic The blood uric acid content at this time was 27 4 mg per cent He was referred to an internist with the diagnoses of recurrent renal calculi and diabetes mellitus Therapy consisted of diet, forcing fluids, sodium bicarbonate and benamid His blood uric acid determination has gradually fallen to 4 4 mg per cent, and the renal colic has not recurred

The second case is that of J C, a white man aged 37, who was admitted to the Harrisburg Hospital on September 24, 1956, with the chief complaints of hematuria and left flank pain Cystoscopy was within normal limits Urine collected from the left kidney was dirty and grossly bloody Intravenous urography and retrograde pyelography revealed a horseshoe kidney, left hydronephrosis and a filling defect within the left renal pelvis The blood uric acid determination was 7 8 mg per cent At operation, on October 2, division of the isthmus of the horseshoe kidney, left nephropexy, and left pelviolithotomy were accomplished Chemical analysis of the calculus revealed it to be composed of pure uric acid Postoperatively the patient was placed on forced fluids, sodium bicarbonate, and benamid His blood uric acid content is now 3 4 mg per cent and his symptoms have not recurred

Group 4 is exactly like group 3, except that the blood uric acid content is within normal limits In our experience, patients with pure uric acid calculi and normal blood uric acid content are perhaps more common than those with elevated blood uric acid determinations Again, we would like to present two typical cases

Mrs M G, a white woman aged 67, was seen in the office on January 23

1957 with the chief complaint of hematuria History revealed that 2 days previously pain developed in the left flank associated with dysuria, frequency every 15 minutes, nocturia, gross hematuria, nausea, and vomiting, chills and fever Examination was essentially negative except for the left flank pain At cystoscopy, the bladder was essentially normal The right ureter was catheterized with ease On the left side, an obstruction was encountered 15 cm up the left ureter and could not be passed with a catheter Retrograde pyelograms revealed a nonopaque obstruction in the left ureter above which a hydroureter was present, and the possibility of a nonopaque calculus was considered She was admitted to the hospital on January 25 with a diagnosis of a nonopaque obstruction in the midportion of the left ureter possibly due to a nonopaque calculus or tumor At the time of admission, no further pertinent facts from the history or physical examination were obtained Laboratory studies were within normal limits The blood uric acid determination was 3 7 mg per cent Intravenous urography revealed that the right kidney functioned normally Definite hydronephrosis was present on the left side with hydroureter all the way down to the bladder The impression was obstruction in the distal portion of the left ureter At cystoscopy on January 28, under intravenous pentothal anesthesia, the bladder cavity was examined and left ureteral meatotomy was done, a stone basket was passed up the left ureter without undue difficulty and a large amount of foul, dirty urine obtained With removal of the stone basket, three yellow calculi were obtained, analysis proved them to be pure uric acid calculi The postoperative blood uric acid content was entirely within normal limits The patient was placed on forced fluids, alkalization of urine, and benamid

K S , a white man aged 34, was admitted to the Harrisburg Hospital on June 1, 1954 with the chief complaint of left flank pain associated with chills and fever Intravenous urography demonstrated a nonfunctioning left kidney, cause undetermined The blood uric acid determination was within normal limits Because the patient had had a commissurotomy during the past year, the possibility of an infected left renal infarct had to be considered Cystoscopy was within normal limits Catheterization of the left ureter demonstrated a hydronephrotic drip of dirty urine Retrograde pyelography revealed a filling defect in the left upper ureter, and a diagnosis of nonopaque calculus was made At operation on June 17, the calculus was easily removed Chemical analysis revealed it to be composed of pure uric acid Convalescence was normal except that the patient had to undergo surgery for removal of the previously described gallstones

A discussion of the differential diagnosis may be best presented by merely listing our cases in which an operation was done because of a filling defect of the upper urinary tract, in which the possibility of uric acid calculi had to be considered

A Papillary carcinoma of renal pelvis, 1 case

B Polycystic kidney disease with no gross deformity of the kidney, 1 case

C Clear cell carcinoma of the kidney with extension to the renal pelvis and no other deformity, 1 case

D Organized blood clot in renal pelvis in polycythemia vera, 1 case

E Precalcareous matrix in renal pelvis as described by Boyce, 2 cases

F Pure cholesterol calculus, 1 case

G Primary carcinoma of ureter, 3 cases

Complications Tubal destruction of the kidneys and various degrees of nephrosclerosis have been adequately described elsewhere However, we should like to emphasize one complication which, to the author's knowledge, has not been stressed in other papers, namely, diabetes mellitus

In our series of patients with uric acid calculi in the past 5 years, which is now well over 50 proven cases, diabetes mellitus has been a complication in approximately 50 per cent

In conclusion, our experiences with uric acid calculi have been presented It has not been our purpose to report anything new or disprove anything old in regard to this problem It is the author's firm conviction that in those patients suffering from renal colic, of undetermined cause, the possibility of uric acid calculi should always be considered, and if the symptoms and laboratory findings are properly analyzed, many disgruntled patients become happy, normal human beings again

803 N Second St , Harrisburg Pa

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THE URINARY AMINO ACIDS IN RELATION TO CALCULUS DISEASE

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Many problems in the pathogenesis of renal calculi remain unsolved It is recognized that calculi are frequently found in association with urinary infection, but many patients with such infection never form calculi Some patients, but not all, who excrete increased amounts of calcium in the urine form stones Some patients suffering from hyperparathyroidism excrete abnormally large amounts of calcium but do not form calculi, although the formation of calculi is a common manifestation of this disease Some patients who repeatedly form stones excrete normal or low amounts of calcium What is the cause of these differences? It has often been postulated that organic substances play a part in holding calcium salts in solution in normal urine substances such as urea, citrate and urinary colloids all having been thought important However the effect of these substances has not been clearly demonstrated The urinary amino acids do not appear to have been considered in this connection According to King,[1] more than 6 gm amino acids are excreted in urine in 24 hours King and Palmer[2] formed a crystalline compound between calcium chloride and L glycine Klement and Weber[3] found that hydroxyapatite was more soluble in solutions of glycine and alanine than in water Lehmann and Pollak[4] reported that amino acids increased the solubility of calcium phosphate These considerations suggested that amino acids might play a part in holding calcium salts in solution in normal urine A study of urinary excretion of amino acids of calculus patients that has been carried out has revealed certain abnormalities, which will be described in a later publication Meanwhile, experiments have been carried out to find out the effect of administration of amino acids to animals on a stone-forming regimen

MATERIALS AND METHODS

Rats weighing from 30 to 40 gm were used for rat experiment 1 Calculi were produced by feeding a diet deficient in vitamin A The diet used is shown in table 1, and is a modification of the diet used by Higgins[5] for production of calculi in rats

Rats were divided into 3 groups, with equal numbers of males and females in each group Group 1 acted as a control group, being fed on the vitamin A deficient

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[5] Higgins, C C The experimental production of urinary calculi J Urol , 29 157, 1933

TABLE 1 *Vitamin A deficient diet*

	Per Cent
Casein	18
Dextrose	35 5
Starch	35 5
Arachis oil	10
Dried brewer's yeast	2
Salt mixture	5
Choline chloride	1

diet without supplements Group 2 was given 10 mg sodium benzoate and 10 mg glycine daily, to increase urinary excretion of hippuric acid (Snapper, Bendien and Polak[6]) Group 3 was given 10 mg DL glutamic acid daily, as in vitro studies suggest that it can prevent precipitation of calcium phosphate (McGeown[7]), and also because human nutrition experiments have shown that this amino acid is increased more than other urinary amino acids by feeding a high protein diet The supplements were given in drinking water, using sucrose as a bait The solutions were adjusted to pH 7 0 before use

Adult mice were used for mouse experiment 1 and 2, male mice in mouse experiment 1 Mouse experiment 2 consisted of equal numbers of males and females in each group, but during the first few days an outbreak of enteritis occurred in cages containing the male animals, and most of these mice died The experiment was continued using females only They were fed on vitamin A deficient diet shown in table 1 Harrison and Harrison[8] have reported that acetazolamide causes calculus formation and renal calcification in rats Accordingly, all mice were given 8 mg acetazolamide (diamox) daily (15 to 20 mg /100 gm body weight) The mice were divided into 3 groups in each experiment, in each of which the first group acted as control and was given diamox only Group 2 in each experiment was given 25 mg DL glutamic acid, and group 3, 3 mg cysteic acid, to increase urinary excretion of cystine Cysteic acid was used because chromatography of human patients' urine has shown that excessive excretion of cystine is a common abnormality in patients who form calcium calculi (McGeown, unpublished data) Diamox and amino acid supplements were given in drinking water, using sucrose as a bait Control groups received diamox and sucrose only

RESULTS

Rat experiment 1 Many rats died during early stages of the experiment from intercurrent infections of the pulmonary or urinary tracts Later the common finding in animals dying was gross urinary infection After the rats had been on the diet for 150 days, calculi began to be found at postmortem examinations

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[6] Snapper I, Bendien W M and Polak, A Observations on the formation and prevention of calculi Brit J Urol, 8 337, 1936

[7] McGeown, Mary G Can renal calculi be prevented? Ulster Med J, 24 129, 1955

[8] Harrison H E and Harrison, H C Inhibition of urine citrate excretion and the production of renal calcinosis in the rat by acetazolamide (diamox) administration J Clin Investig, 34 1662, 1955

TABLE 2 *Rat experiment 1*

Group	No of Rats	Supplement	Calculi Present	Rats with Calculi
				per cent
1	24		7	29 1
2	25	Glycine and sodium benzoate	8	32 0
3	25	DL glutamic acid	0	0 0

For groups 1 and 3 χ^2 = 6 3, 02 > P > 0 01

All rats surviving at 250 days were killed The most frequent site for calculi was the bladder, but occasionally they were present in the renal pelvis The total weight of calculus in an individual rat varied from 0 6 mg to 395 mg The major inorganic cation of the calculi was calcium, which amounted to 20 per cent of the total weight in some specimens The results are shown in table 2 Calculi occurred among control rats, and among those given glycine and sodium benzoate, but there were no calculi in group 3 which had received glutamic acid

Mouse experiment 1 The mice in this experiment were killed after 4 weeks The results are shown in table 3 At autopsy some mice had tiny calculi in the bladder The kidneys and bladders were x-rayed, and in addition to vesical calculi, a few of the kidneys showed calcification along the cortico-medullary junction, radiating towards the pelvis as little streaks Calcification of the kidneys, sometimes but not always, occurred in mice having bladder calculi Bladder calculi and renal calcification are listed separately in tables 3 and 4

Table 3 shows that fewer mice formed bladder calculi in group 2, which received glutamic acid, than in the other 2 groups Calcification of kidneys occurred infrequently in all groups, but was more frequent in group 3 than in other groups Numbers of mice having renal calcification were too small for tests of significance to be applied

TABLE 3 *Mouse experiment 1*

Group	No of Mice	Supplement	Bladder Calculi		Renal Calcification	
			No	Per cent	No	Per cent
1	17		6	35	1	6
2	19	DL glutamic acid	1	5	1	5
3	20	Cysteic acid	2	10	3	15

For groups 1 and 2 χ^2 = 4 5, 05 > P > 02

TABLE 4 *Mouse experiment 2*

Group	No of Mice	Supplement	Bladder Calculi		Renal Calcification	
			No	Per cent	No	Per cent
1	21		12	57	2	9 5
2	21	DL glutamic acid	4	19	2	9 5
3	12	Cysteic acid	4	33	2	16

For groups 1 and 2 χ^2 = 4 6, 05 > P > 02

Mouse experiment 2 The mice in this group were killed after 5 weeks' treatment with diamox and other supplements The results are shown in table 4 Vesical calculi were again less numerous in group 2, which had received glutamic acid, than in either the control group or the group which had received cysteic acid

Renal calcification was less frequent than bladder calculi, but again occurred most often in group 3, which had received cysteic acid The increased frequency of bladder calculi in all groups in this experiment was probably due to the fact that treatment with diamox was more prolonged

DISCUSSION

The experiments described here have shown that administration of glutamic acid prevented formation of calculi in rats fed on a vitamin A deficient diet Glutamic acid treatment also significantly reduced the incidence of calculi in mice given diamox The action of glutamic acid does not appear to be due to increased acidity of the urine because no difference in urine pH was found between groups given glutamic acid and controls Furthermore the solutions were adjusted to pH 7 0 before use Glutamic acid may form a soluble compound with calcium, perhaps a chelate compound, and thus help to prevent precipitation of calcium salts, but as yet there is no direct evidence of its mode of action It may act in some indirect way, perhaps taking part in the formation of a polyelectrolyte, which may be more active in binding calcium ions (Gregor[9])

Administration of sodium benzoate and glycine was recommended by Snapper, Bendien and Polak[6] for the prophylaxis of recurrent calculi, after they had found that the addition of sodium benzoate prevented calculi in rats fed on a diet containing a high proportion of calcium carbonate They reported that it cleared the urine of patients with phosphaturia Cook,[10] Kearns[11] and Burkland[12] also recommended sodium benzoate and glycine for the prophylaxis of recurrent calculi Keyser[13] did not think it prevented recurrences in rapidly stone-forming kidneys although it cleared crystalluria In the present experiment the administration of sodium benzoate and glycine did not reduce the number of vitamin A deficient rats forming calculi

Cystinuria was a frequent finding in human patients who formed calcium stones (McGeown, unpublished observations) Mice were given cysteic acid to increase urinary excretion of cystine to see if this affected the incidence of calculus formation There was no increase in incidence of calculi in mice given cysteic acid, although it did not decrease calculus formation as did glutamic acid Renal calcification appeared to be more frequent in mice given cysteic acid, but the number of mice involved was too small for the results to be considered significant

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[12] Burkland C E Etiology and prevention of oxalate calculi in the urinary tract J Urol 46 82, 1941

[13] Keyser L D Urinary lithiasis J Urol, 50 169 1943

Further experiments are in progress to determine whether the oral administration of amino acids to rats increases the amount excreted in the urine

These experiments do not prove that a diminished urinary excretion of amino acids is the cause of calculus disease in human patients, but they suggest that amino acids may play a part in pathogenesis of this disease We would like to discover whether glutamic acid can prevent the formation of calculi in patients who are particularly prone to form recurrent stones, but it has not yet been possible to obtain a supply of glutamic acid sufficient for treatment over a period of years We are treating a series of such patients with a high protein low calcium diet, but as yet the followup period is not long enough for any conclusion as to its effect

This work was accomplished during tenure of grant from the Medical Research Council I am grateful to Professor G M Bull for advice in carrying out the work The firms of Roche Products Limited and Lederle Laboratories kindly supplied glycine and glutamic acid

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ECHINOCOCCOSIS OF THE KIDNEY

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Human echinococcosis or hydatid disease is caused by the parasite Taenia echinococcus, or dog tapeworm. This is the most dangerous of all the human tapeworm infestations.

INCIDENCE

Hydatid disease is rare in North America. In the pastoral countries, especially the sheep-raising areas, it has become a common disease. This high incidence can be gauged by Barnett's estimate of the new cases of hydatid disease per annum in the following countries:

	Cases
Uruguay	400
Argentina	300
Australia	200
New Zealand	120
South Africa	80

Kidney involvement is quite uncommon; it probably represents 2–3 per cent of all hydatid cases.[1-4] Up to 1954, fewer than 40 cases of renal hydatid had been reported in the United States.[2, 4]

PATHOGENESIS

The adult Echinococcus, a cestode of the Taenia family, lives in the folds of the small intestine of the dog. It is 5–8 mm. long, and consists of a rounded head with a double row of hooklets and a ribbon-like body. Although a variety of pastoral animals may act as intermediate host, human infestation generally occurs from the ova in dog's excreta. Contaminated food, water, or finger contamination (especially in children) introduce these ova into the human digestive tract. These eggs, containing the hooked embryo, hatch in the human small intestine. Almost immediately the six-spined embryo burrows through the mucosa into the mesenteric venous system. The liver acts as the first "filter" of the portal vessels; 70 per cent of human lesions occur in the liver. If the embryo escapes liver lodgement, it is apt to be arrested in the lungs; 12 per cent of lesions are found in pulmonary tissue. If the lungs fail to remove it from the blood, any other part of the human body can become the seat of arrest and growth (renal tract, bones, muscles, and central nervous system).[5]

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Baurys, W.: Echinococcus disease of the kidney. J. Urol., 68: 411–446, 1952.

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Once located in a tissue, the embryo vies with the host's resistance mechanism for survival, many an embryo probably loses the battle In 40 per cent of infested humans, a single solitary cyst is found, likely a lone survivor of numerous tissue implants [6] With survival, a foreign body type reaction is stimulated, followed by vesiculation, central fluid, and cyst formation

The adult cyst has an outer layer or adventitia which is an intimate part of the host tissue Within is the laminated germinating membrane, which protects the growing scolices Fluid secretion slowly enlarges the cyst, in kidney tissue a diameter of 10 cm may be reached in a year [7] [8] Generally, however, cyst growth in the kidney is very insidious The renal hydatid may become latent and inactive, with thickened and calcified adventitia Activity will lead to daughter cysts within the lesion, with continued growth Rupture of the cyst leads to infection and possible implantation of daughter lesions in other parts of the urinary tract Scolices may be extruded by way of the urine

PATHOLOGIC AND ROENTGEN FEATURES

Renal hydatid involvement is generally primary and blood-borne Rarely, the kidney becomes involved through direct extension of a hydatid from the liver or spleen Since the hydatid cyst will grow in the direction of least resistance, anterior growth usually ensues Renal enlargement occurs, but rarely is the kidney displaced The growing cyst may displace and distort the calyceal system, much like a simple serous cyst It may simulate a neoplasm, stretching and even obliterating some calyces In time, many (25 per cent) of the lesions will undergo adventitial calcification

Roentgenologically, the closed cyst will generally produce enlargement of the renal shadow, anteriorly Calyceal distortion is common, and may simulate a simple cyst or neoplasm The calcification will frequently raise the suspicion of tuberculosis

In open cysts, the opaque medium may spread around the cyst, giving rise to the so called 'wine-glass' shadow [1] If the 'dye' enters the cyst, an opaque mass with small negative shadows (daughter cysts) may be seen In the absence of daughter cysts, the dye filled cavity communicating with the calyces may simulate a renal carbuncle

SYMPTOMS AND DIAGNOSIS

The symptomatology of renal hydatid is nonspecific A closed cyst may be completely asymptomatic It is thought that an average of 20 years elapses between renal hydatid infestation and the development of clinical features Calyceal impingement may lead to renal colic or recurrent renal pain of lesser intensity

Once the cyst becomes open, a fairly large variety of distressing symptoms may occur Renal infection will manifest itself with usual findings, renal colic, hematuria and dysuria are not infrequent Acute rupture of the cyst may simulate an acute process in the abdomen[7] The open type may prove fatal, if untreated

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The diagnosis of hydatid cyst of the kidney is rarely made in the United States,[4] primarily because of a low index of suspicion The possibility of hydatid disease should be considered in the presence of a calcified kidney mass Bauer,[9] writing on renal calcifications, includes tuberculosis, gummatous masses, infarcts, coagulated blood collections, tumors, cysts, and Echinococcus disease in the differential diagnosis In renal infarction, however, calcification is most unusual[10] The calyceal distortions on pyelograms are in themselves not specific In open cysts, the 'wine-glass' sign or the defects in the dye-filled cavity may suggest the diagnosis A previous history of hydatid disease will naturally heighten the suspicion from the roentgen findings The identification of hydatid elements in the urine, of course, will establish the diagnosis[7, 11, 12] Significant eosinophilia will be found in only 25 per cent of patients infected with Echinococcus Immunologic responses of the host may be utilized diagnostically These include the precipitin (Casoni reaction), complement fixation (Weinberg), and the skin tests, using fresh cyst fluid The latter have been reported positive in the majority of proven cases[13] Immunologic reactions may be completely absent where the cysts are of long-standing inactivity or completely burned out

PROGNOSIS AND TREATMENT

The closed cyst, becoming burned out and inactive, remains unchanged and asymptomatic indefinitely Calcification usually occurs, and the accidental finding of a calcified hydatid cyst of the kidney would appear to necessitate no treatment Generally, surgical excision is performed, and diagnosis of hydatid made by the pathologist Medical diagnosis of a closed renal hydatid cyst is rarely made without surgery

If large enough, the cyst may compress and block calyces, and cause caliectasis and infection Nephrectomy is the sole curative measure Open cysts commonly will terminate fatally if nephrectomy is not performed

Some authors have attempted x-ray therapy for cyst due to the Echinococcus[14, 15] Fairly large doses (up to 1200 roentgens of 200 KVP per portal) appear to destroy the fertility of the eggs, inhibiting or arresting activity of the cyst This effect is most favorable in early lesions[15]

CASE REPORT

S D , a 78-year-old man, was admitted to the medical service at Kensington Hospital because of pain in the left lumbar area The pain had suddenly started two days before admission, and subsided after a few hours It recurred severely the day of admission

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[13] Hudson P I Echinococcus disease South Med J , **38** 584-589, 1945

[14] Dorrance G M and Bransfield J W Recurrent echinococcic cysts of liver treated by deep x ray therapy Am J Trop Med **27** 27-77, 1947

[15] Gerulewicz L Radiation therapy of Echinococcus alveolaris of liver Radiol Clin , **15** 230-235 1946

The patient had no history of previous significant illness Born in England, he had migrated to this country at age 33, and had been steadily employed as a weaver in a carpet factory until the initial attack of pain As far back as he could remember, one dog or another had been a constant household pet

The patient was well nourished He complained bitterly of pain in the left side of the abdomen and flank Definite tenderness was elicited over the left flank, but the rest of the physical examination uncovered no other significant abnormalities No elevation of blood pressure was found The blood studies were all within normal limits, no eosinophilic cells were noted on the smear (Blood urea nitrogen 14, hemoglobin 12 5, white blood cells 8,000) A tentative diagnosis of renal colic and calculus was made The urine, however, contained no red blood cells, although numerous pus cells were found

Excretory urography revealed a normal right urinary tract, the left kidney was enlarged and excreted no dye Mottled calcifications were seen in the left kidney area, a lateral view (fig 1) revealed a crescentic, linear calcification involving practically the entire anterior border of the kidney, which was considerably expanded anteriorly The left retrograde pyelogram revealed marked hydronephrosis The calyces were severely dilated, blunted, and a cresentic depression was noted on one upper calyx (fig 2) The ureter was moderately dilated with irregularities in the upper half Although no tubercle bacilli could be isolated from the urine, a tentative diagnosis of renal tuberculosis was made All urine cultures were repeatedly negative Chest roentgenograms were negative

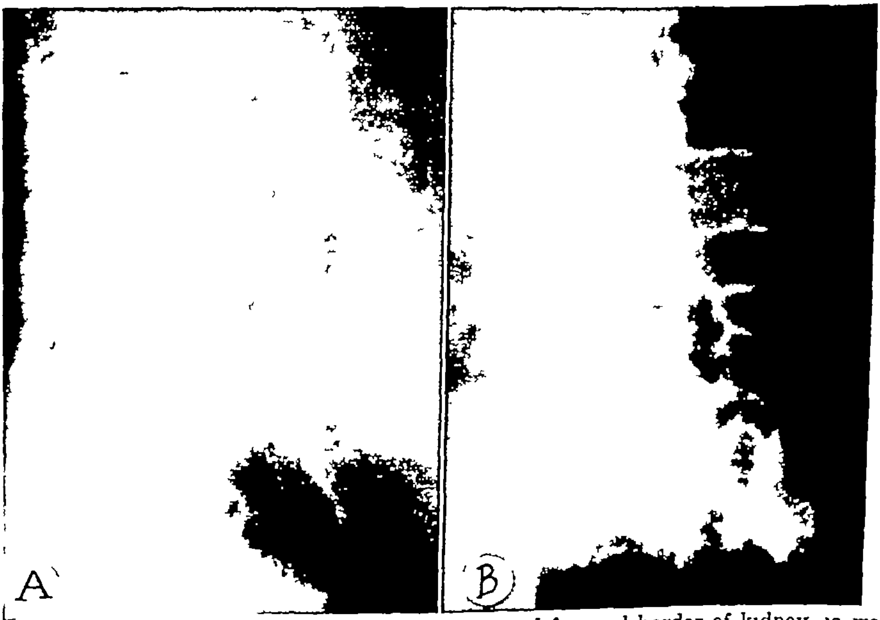

FIG 1 Curvilinear, calcified shell, anterior to usual forward border of kidney, is well demonstrated only on lateral view *B*, anteroposterior films contained too much gas to delineate faint mottled calcifications

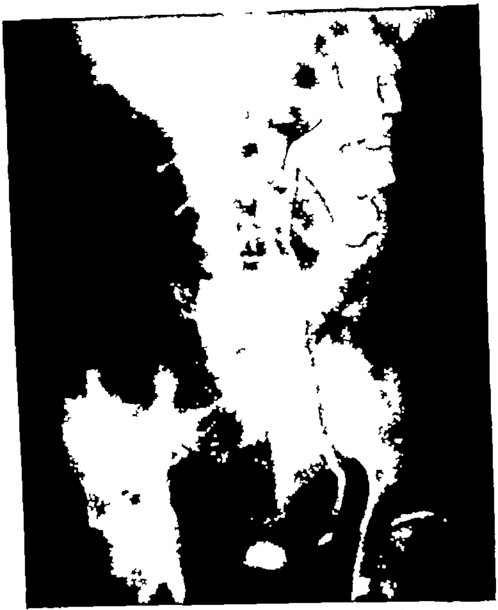

FIG 2 Flattening, broadening and dilatation of pelvis and calyces are not due to obstruction of ureter, but to pressure deformity from large anterior renal mass

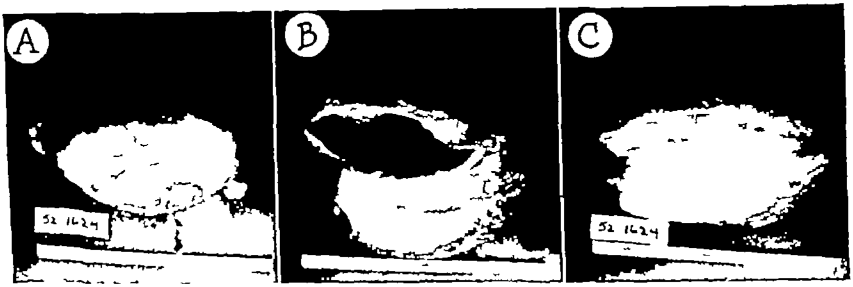

FIG 3 *A*, intact kidney, note enlargement *B*, cystic cavity, note paper thin wall at numerous points *C*, gelatinous mucoid material of mother cyst admixed with daughter cysts

At surgery, a calcified shell was found around the kidney, anteriorly Many adhesions had to be freed and the kidney was removed The renal pedicle was treated in the usual manner The pathological report (Dr A I Rubenstone) indicated an intact, globullary, enlarged kidney measuring 15 by 9 by 9 cm, and weighing 750 gm The medial-anterior aspect contained an elliptical, yellowish-pink area 9 by 8 cm, calcareous plaques were present on a roughened surface Section revealed a cystic cavity 11 cm in diameter, with a paper-thin wall in many areas A gelatinous mucoid material filled the cavity, admixed with a number of globular cyst-like structures Watery fluid filled these small cysts The renal pelvis was displaced posteriorly and the renal parenchyma was compressed around the cyst (fig 3) Microscopic examination showed large expanses of well-preserved renal parenchyma Focal collections of lymphocytes and eosinophils were associated with some parenchymal fibrosis, tubular atrophy,

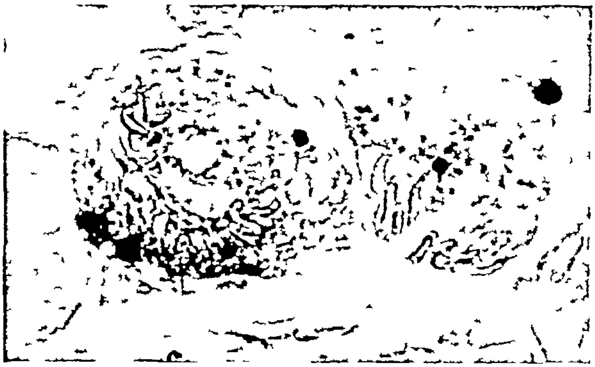

FIG 4 Characteristic histologic picture of echinococcosis, with hooklets

and occasional glomerular sclerosis The wall of the large cyst was fibrotic and hyalinized The cyst was multilocular and contained the hooklets characteristic of Echinococcus (fig 4)

The postoperative course was stormy, and a severe bout of ileitis threatened recovery However, under conservative management, the patient was discharged well on the twenty-fifth postoperative day

DISCUSSION

The onset of symptoms at age 78 is most unusual Our patient was many years older than any of the reported cases in the American literature Though asymptomatic until a few days before surgery, the renal lesion undoubtedly was of long standing, as evidenced by its size and complete anterior calcification (fig 1)

The patient had lived in England until age 33 and always had possessed household dogs The renal hydatid probably had its origin in one of the infested pets

The abrupt clinical onset of renal colic, with no antecedent renal history is a little unusual, particularly since this was a closed cyst However, the pressure, stretching, and distortion of the pelvis and calyces (fig 2) could account for renal pain No apparent function of this kidney was demonstrated by intravenous urography The picture produced by retrograde pyelography was nonspecific, since no dye could enter the cyst cavity to demonstrate defects from daughter cysts The anterior location of the lesion and the calcification are, however, fairly typical of renal hydatid The diffuse pressure on the anterior renal parenchyma suggested malignant lesion, even at surgery

It is of interest that clinically, roentgenologically, and surgically no other tissue hydatids were uncovered The majority of patients with renal hydatid show cysts elsewhere [5]

Since echinococcosis was not suspected, precipitin and complement-fixation tests were not considered No eosinophilia was even found The preoperative diagnosis was renal tuberculosis Complete cure was obtained by surgery

In retrospect, the following features of the case were fairly characteristic for diagnosis of renal hydatid 1) a long sojourn in England, and intimate association with dogs, 2) renal colic, 3) roentgen demonstration of a large anterior renal mass, with a calcified anterior wall, and with flattening, broadening, and dilatation of pelves and calyces, 4) nonfunctioning kidney, revealed by intravenous urogram

The less usual features included the advanced age of the patient at onset, complete symptom-free prior existence, and the absence of any other demonstrable hydatid lesions

CONCLUSIONS

A case of proven echinococcosis of the kidney is presented Fewer than 40 cases have been reported in the United States

The patient, with symptom onset at age 78, is the oldest in the American literature

The cyst was of the closed type, and as such, presented the characteristic roentgen features of a large anterior renal mass, with a calcified anterior margin, and with evidence of severe pressure effects on the renal pelvis and parenchyma

Surgical ablation of the involved kidney provided a clinical cure

The clinical, roentgen, and the pathologic features of echinococcosis of the kidney are reviewed

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BENIGN OSSIFIED LESION OF THE KIDNEY—REPORT OF A CASE RESEMBLING A HYDATID CYST

HENRY G MISHALANY AND DONALD R GILBERT
From the Urological Service, Memorial Hospital, Charleston, W Va

The occurrence of bone formation in benign lesions of the kidney is rare Most textbooks of pathology contain no specific reference to this condition It is well known however that heterotopic bone formation may take place in any tissue containing long-standing deposits of calcium Dead or damaged tissue, chronic inflammation and hemorrhage "so large or so situated that they cannot be absorbed" invite the deposition of calcium salts in localized areas (Goldstein and Abeshouse) This pathologic calcification is an independent local process, distinct from the diffuse calcium deposition in one or several organs resulting from a systemic physiologic imbalance in calcium and phosphorus metabolism (Moore) The process of heterotopic bone formation in such tissues has been the subject of debate From the many theories advanced the most plausible seems to be the one of Leriche and Policard These investigators pointed out that fibroblasts revert to osteoblasts under certain conditions and thus form true bone Huggins presented experimental evidence in animals to support this theory

True bone formation in malignant lesions of the kidney is not common and has been adequately reported elsewhere (Austin, Goldstein and Abeshouse) Although calcium deposition in malignant renal lesions is frequent (around 15 per cent), the relatively rapid course of events in the majority of cases precludes ossification

BENIGN OSTEOMAS

Marion reviewed the benign osteomas of the kidney and reported one case, he referred to four others He stated that renal osteomas "present themselves as a round tumor making a bulging under the capsule of the kidney from which they arise and are composed of osseous tissue " Kretschner presented a case, and reviewed the possible methods of origin of pararenal osteomas quoting the criteria and theories of Virchow, Ewing, Wooley and Mallory

TRAUMA

A benign bony tumor may result from organization of blood and urine occasioned by trauma to the renal area This has been referred to by Colston

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Ossified endotheliomas of the kidney have been reported Ponzio presented a case where the osseous formation disclosed the characteristic structure of a vein with preservation of all the layers of the wall

The literature abounds with evidence of bone production following the experimental ligation of the renal vascular pedicle (Sacerdotti and Frattin) Schmorl

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reported an unusual case where the complete interference with the blood supply of the kidney caused bone formation beneath the mucosa of the renal pelvis

INFLAMMATION AND INFECTION

Bone formation may result from organization of an inflammatory process in and around the kidney Hydronephrosis, pyonephrosis, abcesses, acute and chronic nephritis are all known to be associated oftentimes with calcium deposition Many such kidneys were reported to show true bone formation (Goldstein and Abeshouse)

While pathologic ossification in other organs of the body due to tuberculosis has been noted we were able to find only one reference by Phemister to bone formation in the kidney occasioned by tuberculosis

RENAL CALCULI AND BONY PELVIS

Osseous metaplasia of the pelvic epithelium associated with renal calculi has been reported by many authors, Phemister in 1923 being the first to call attention to this association

CYSTS

Several instances of bone formation have been described in cases of dermoid cysts and solitary cysts of the kidney, the latter mostly being autopsy findings

Approximately one-fourth of the hydatid ecchinococal cysts of the kidney contain sufficient calcium in the cyst wall to be demonstrated roentgenologically (Ray and Rolleston) Renal hydatid disease is uncommon in the United States Berger in 1954 reported the thirty-seventh case in the literature Few authors refer to bone formation in hydatid cysts and none have been reported in this country Dickinson stated that many preparations in English museums showing formation of bony hardnesses within the kidney appear to be derived from transformation of hydatids Bernardi from Argentina has the only reported case in the recent literature of a calcified and ossified hydatid cyst of the kidney His case was known to have had the tumor for the past 30 years The intradermal Cassoni test was negative (no reference to the Weinberg complement fixation was made) The cyst was as big as "a human head" and had an outer bony covering of 2–4 mm in thickness It contained a dark yellow, odorless fluid with some daughter cysts

CASE REPORT

M M, No 33690 A 27-year-old white woman was admitted to Memorial Hospital on March 16, 1956 with the chief complaint of pain in the right upper abdomen of 2 years' duration The pain was cramping in nature, intermittent in character and intensity and lasted from a few minutes to several days On occasion there was associated nausea and vomiting Sedations and recumbency were necessary to relieve the pain The patient gave no history of food intolerance, change of bowel habits, or blood in the stools There was no nocturia dysuria, hematuria increased frequency of urination or radiation of pain simulating renal disease There has been no loss of weight or strength The patient lived on a farm

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Physical examination revealed a thin young woman with no acute complaints The only abnormal physical findings were localized to the right upper abdominal quadrant where a hard, smooth, nontender mass could be palpated The mass was easily outlined, measured 6–7 cm in diameter and moved slightly downwards with inspiration It was distinct from the liver and felt to be in intimate proximity to the right kidney The left kidney felt normal

Laboratory data Hemoglobin 13 8 gm , white blood cells 10,200 with 70 per cent neutrophils, 26 per cent lymphocytes, 3 per cent monocytes, and 1 per cent eosinophils The sedimentation rate was 11 mm in one hour The blood urea nitrogen was 15 mg per cent The serological test for syphilis was negative Urinalysis specific gravity 1 010 with normal microscopic albumin and sugar determinations Bladder urine culture yielded a light growth of Staphylococcus albus

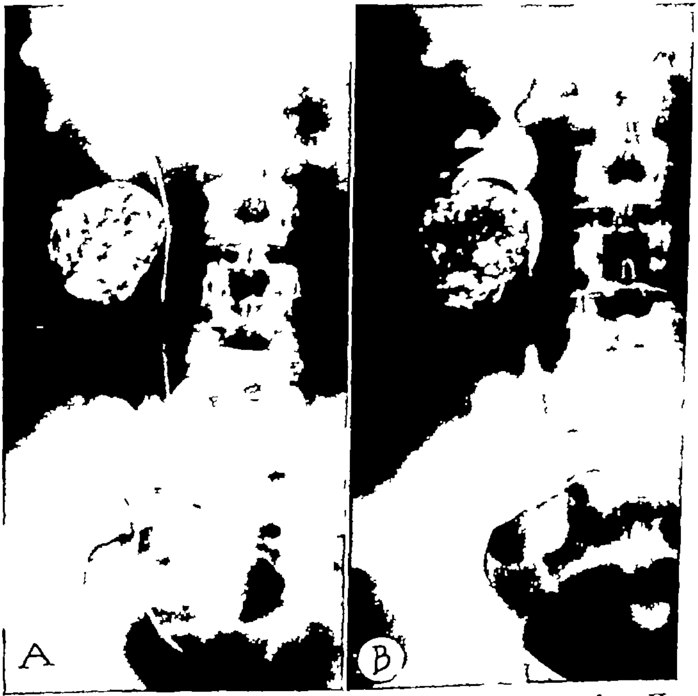

FIG 1 A, plain film of abdomen with right ureteral catheter in pelvis Honeycombed, densely calcified mass is at lower pole of right kidney B, intravenous urogram shows good concentrating function but flattening of lower calyx of right kidney

Cystoscopic examination disclosed a normal bladder with no obstruction to the passage of catheters to the kidneys Functional renal studies were normal and the pelvic urines were bacteriologically sterile

X-ray examinations showed normal lung fields The series of gastrointestinal films were normal The plain film of the abdomen (fig 1, *A*) revealed a conglomerate area of calcification in the lower pole of the right kidney which measured 6½ by 5½ cm No other calcifications were noted Excretory urograms and retrograde pyelograms confirmed the location of the calcified mass and demonstrated no functional change in either kidney (fig 1, *B*)

Right nephrectomy was accomplished March 20, 1956 through the lumbar approach There was no evidence of perirenal inflammatory reaction or increased vascularity The lesion involved the lower half of the kidney and was entirely within the renal capsule Its firmness was that of bone Nephrectomy was elected and performed because of the indefinite nature of the lesion and the fact that partial nephrectomy would have left less than half the renal substance

The patient's postoperative course for six months has been uneventful

Section of the kidney revealed that the upper half was grossly normal, but a bone saw was required to bisect the tumor (fig 2) An outer layer of bone measured 5 mm in thickness with bony trabeculations enclosing several cystic spaces, some multiloculated ranging from ½ cm to 2 cm in diameter (fig 3, *A*) Clear fluid was present in the cysts, culture was negative for acid-fast organisms No attempt was made to search for scolices or hydatid sand

One month postoperatively a Weinberg complement fixation test was performed and reported as negative No test material was available to perform the Casoni intradermal test

Pathological report 'The gross specimen comprises a kidney weighing 200 gm and measuring 13 by 6 5 by 5 5 cm The capsule strips with relative ease over

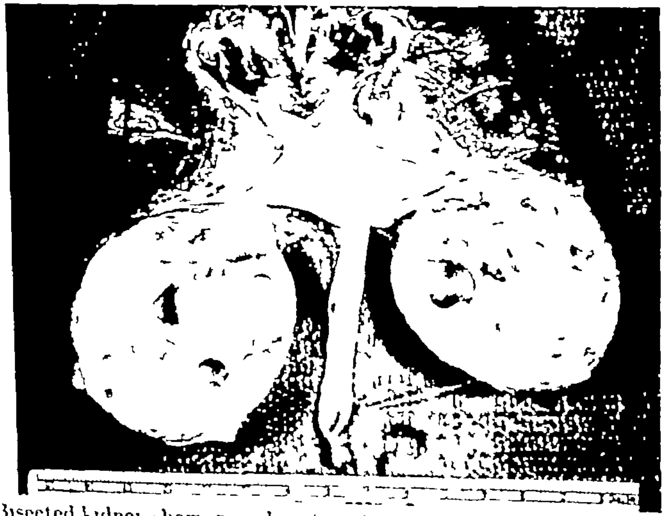

Fig 2 Bisected kidney shows round cyst containing small cystic spaces filled with clear fluid

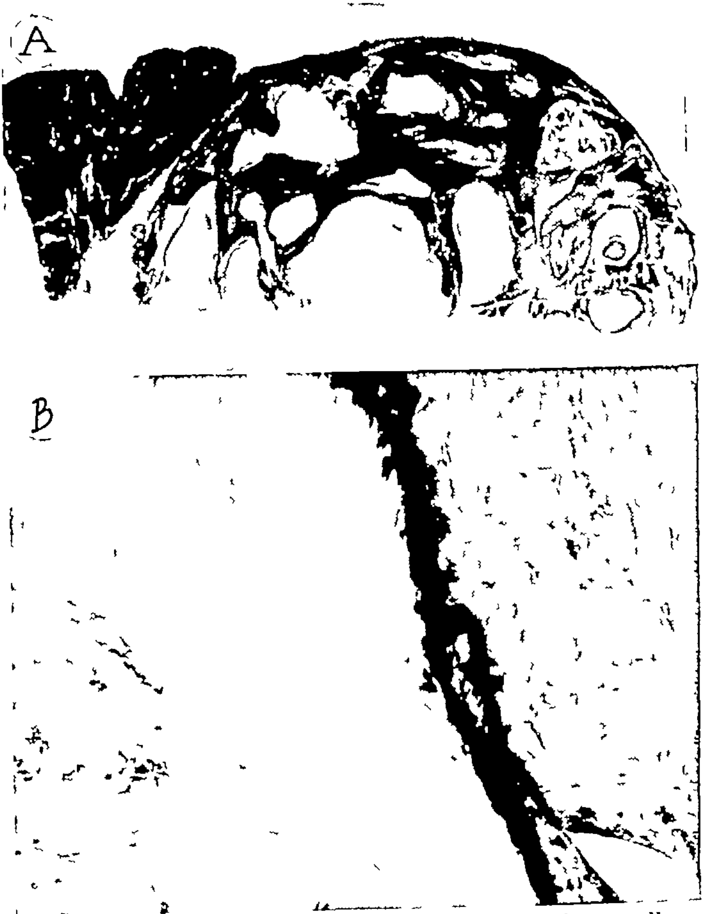

FIG 3 *A*, cross section of cyst shows bony trabeculae surrounding small cysts *B*, microscopic section of bone with bone marrow elements

most of the renal surface except at the lower pole where it is partially adherent to a fissure between the renal substance and a spherical tumor mass measuring 5 5 cm in greatest dimension This tumor mass reveals an extremely hard consistency resembling bone and displays a cystic structure on section The renal tissue per se presents a uniform reddish-brown appearance while the tumor at the lower pole shows a variegated coloration In some areas there is a grayish-white appearance, in others a yellow or orange color The cysts on the surface of the sectioned tumor vary in size up to 2 cm The cortical and medullary demarcation in the uninvolved renal tissue is sharp The inferior major calyx is markedly compressed by the tumor It cannot be ascertained with certainty whether or not the renal substance and calyceal system are actually incorporated within the tumor A segment of ureter approximating 4 5 cm in length is attached The wall is slightly thickened No other changes are observed "

Microscopic description (fig 3, *B*) "The renal tissue reveals relatively undisturbed parenchyma in most places There are occasional foci of calcific deposition in the inner cortex and outer medulla, chiefly in the vicinity of blood vessels The major mass described grossly consists of a portion of tissue which is apparently intraparenchymal with relation to the kidney per se This mass is composed of an outer wall of dense fibrous tissue showing little inflammatory reaction, but occasional atrophic colloid filled renal tubules The major portion of the mass is composed of moderately well formed osseous tissue and densely packed hyalinized collagenous tissue The bone shows well formed trabeculae and numerous growths of bone marrow The marrow shows no abnormal cellular changes No positive evidence of parasitic tissue (e g Echinocococcus) is found There is no evidence of a basic underlying epithelial neoplasm There is likewise no evidence of cellular anaplasia "

Diagnosis "Heterotopic ossification, kidney While the exact etiology and pathogenesis of this lesion at the present time must remain obscure, the gross morphology suggests an underlying lesion such as an old echinococcosis infestation or possibly a cortical adenoma subsequently calcified and ossified "

DISCUSSION

The pathological report of probable hydatid cyst of the kidney was the diagnosis of Dr V E Martins and concurred in by consultants at the Armed Forces Institute of Pathology in Washington, D C The diagnosis was mainly based on the gross appearance of the cyst, as the microscopic study was noncontributary In the early stages of hydatid disease eosinophilia is commonly present and the Weinberg complement fixation test positive, especially if there is leakage from the cyst (Ray and Rolleston) In the case presented, eosinophilia was absent and the Weinberg test negative The disease is so rare and sporadic in the United States that most public health laboratories unfortunately are unable to obtain fresh hydatid fluid to perform the more reliable Casoni test

The possibility of the cyst presented being an organized, calcified and ossified hematoma following trauma is considered unlikely The mild nature of the trauma reported as well as the gross structure of the cyst are inconsistent with this diagnosis It is recognized that this lesion could be an ossified cortical adenoma

SUMMARY

A brief review of the literature regarding benign bone growths of the kidney has been presented

A case showing a solitary ossified cyst of the kidney resembling a hydatid echinococcal cyst has been presented and discussed

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THE EFFECT OF CORTISONE ON EXPERIMENTAL HYDRONEPHROSIS FOLLOWING URETERAL LIGATION*

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The observations reported here were made in the course of experiments involving the effect of ureteral obstruction on susceptibility to infection in the kidney of the rat It was noted that treatment with cortisone altered considerably the anatomic changes in the kidney following ureteral ligation

METHODS

A) Animals White, male, Sprague-Dawley strain rats weighing 150–250 gm were used Purina Chow cubes and water were available at all times

B) Ligation of the ureter The animals were anesthetized with 10–12 mg pentobarbital sodium administered intraperitoneally, supplemented as necessary After hair of the left flank area was removed with electric clippers and operative site cleansed with 70 per cent ethyl alcohol, a 2 cm incision was made just below and parallel to the lower rib margin on the left A small segment of ureter, approximately 2 cm from the ureteropelvic junction, was freed from surrounding tissues and ligated with silk thread The peritoneum was approximated with interrupted silk sutures and the skin wound closed with metal clips

C) Cortisone administration The animals received 6 25 mg of cortisone acetate suspended in saline (cortone acetate, Merck) per day, subcutaneously, in one injection, beginning on the day of ureteral ligation Groups of these rats were sacrificed at 4 8 and 15 days and their kidneys studied Control groups of animals were not given cortisone and were ligated and sacrificed at the same intervals

D) Removal of kidneys for study The animals were anesthetized with intraperitoneal pentobarbital sodium, and a midline incision made The right and left renal blood vessels were clamped simultaneously, then cut medial to the clamps, ureters were cut below the level of ligation, and kidneys removed, photographed and weighed A small cut was then made in the pelvis of the obstructed kidney, allowing fluid in the pelvis and upper segment of ureter to drain by gravity and the kidney weighed again The organs were placed in neutral formalin (10 per cent) and after fixation sections were stained with hematoxylin and eosin

RESULTS

In situ, the obstructed kidneys in animals which received cortisone appeared more nearly the same color as the unobstructed kidneys than was the case in the control group, in which a bluish discoloration is characteristic During the second week of complete ureteral obstruction varying amounts of perinephric

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† Research Fellow of the American Heart Association

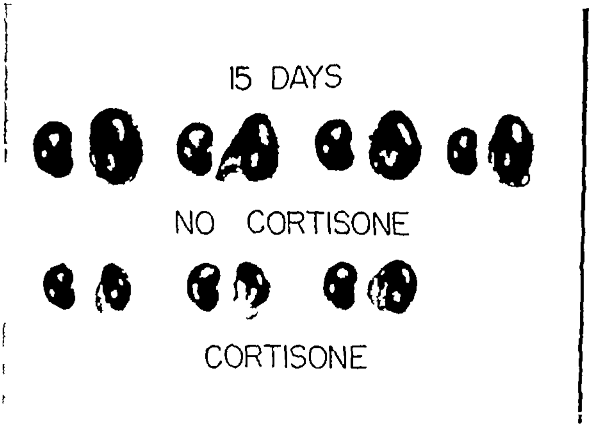

FIG 1 Pairs of rat kidneys 15 days after ureteral ligation was performed on left Note difference in size between group receiving cortisone and controls

edema develops, frequently accompanied by formation of adhesions between obstructed kidney and surrounding structures These perinephric changes were less marked in groups treated with hormone Another finding was an increased amount of bleeding from perinephric tissues in cortisone-treated animals at time of removal of kidneys This was rarely observed in controls

In 7 rats examined 15 days after ligation, a marked difference was detected, in that obstructed kidneys of animals treated with cortisone appeared smaller than those of control animals (fig 1) Weights of kidneys of this group of animals, given in table 1, show that the ratio of weight of hydronephrotic kidney to normal kidney (A/C ratio) was 1 47 or less in the cortisone-treated group whereas it was 2 50 or greater in controls ($p < 01$) Animals receiving cortisone accumulated less hydronephrotic fluid than controls Thus, if weight of intact obstructed kidney minus weight after fluid has been removed (A minus B) is used as an estimate of amount of hydronephrotic fluid present, then animals receiving cortisone had 0 21 gm or less of fluid while controls had 1 56 gm or more ($p < 01$) As subsequent microscopic examination revealed, this is due to accumulation of hydronephrotic fluid within dilated renal tubules as well as interstitial edema, both of these being less prominent in cortisone-treated animals Changes in kidneys of animals sacrificed at 8 days were similar to those noted at 15 days but were less marked No significant changes were noted in rats studied at 4 days

Rats sacrificed at 8 and 15 days demonstrate another finding, unobstructed kidneys in animals which received cortisone weighed less than similar kidneys in controls This change was not apparent in animals studied at 4 days However, these differences were not statistically significant when analyzed in terms of body weight

Microscopic examination revealed differences compatible with macroscopic findings At 15 days, obstructed kidneys in the control group had cystic dilatation of tubular systems, at times severe enough to prevent identification of particular tubular segments (fig 2) Epithelial cells were flattened and in areas

TABLE 1 *Comparative weights of kidneys in rats with and without cortisone treatment*

Rat No	Days Obstructed	Cortisone (mg /day)	Initial Body Weight (gm)	Final Body Weight (gm)	Weight of Obstructed Kidney (gm)		Weight of Unobstructed Kidney (C)	(A) Minus (B)	A/C Ratio
					Pelvis intact (A)	Pelvis drained (B)			
1	4	6 25	—	—	1 65	1 30	0 80	0 35	2 06
2					1 95	1 50	1 10	0 45	1 77
3					1 18	1 00	0 88	0 18	1 34
4					1 25	1 05	0 80	0 20	1 56
1		0	—	—	2 14	1 72	0 98	0 42	2 18
2					1 30*	1 20	1 07	0 10	1 21
3					2 25	1 82	1 04	0 43	2 16
4					1 72	1 30	0 85	0 42	2 02
1	8	6 25	158 0†	155 5	2 61	1 71	1 11	0 90	2 35
2			171 0	161 0	1 90	1 33	0 92	0 57	2 07
3			159 0	152 0	1 30	1 14	0 86	0 16	1 51
4			140 0	—	1 19	1 06	0 81	0 13	1 47
5			168 0	162 0	2 25	1 63	1 20	0 62	1 88
1			193 5†	199 0	2 89	1 96	1 05	0 93	2 75
2			175 5	191 5	2 75	1 75	1 06	1 00	2 59
3			185 5	196 0	3 00	2 03	1 01	0 97	2 98
4			216 5	226 0	—	1 47	1 13	—	—
1	15	6 25	245 0	180 0	1 04	0 89	0 90	0 15	1 16
2			238 0	177 0	1 10	1 06	1 01	0 04	1 09
3			247 0	173 0	1 56	1 35	1 06	0 21	1 47
1		0	243 0	291 0	5 07‡	2 01	1 68	3 06	3 01
2			230 0	271 0	3 47	1 81	1 39	1 66	2 50
3			234 5	260 0	3 66	1 87	1 46	1 79	2 51
4			257 0	221 0	3 19	1 63	1 02	1 56	3 12

* No evidence of ureteral obstruction found at autopsy This is believed to be due to a technical error in ligation

† These weights are not initial weights but were obtained 4 days after ureteral ligation

‡ Abscess in renal cortex

had undergone degenerative changes Between dilated tubules were islands of compressed segments and occasional areas where tubular structure was being replaced by fibrous tissue The papillae of these animals showed atrophy of tubular elements associated with minimal polymorphonuclear and round cell infiltration Rat No 1 in this group had a large acute abscess at the corticomedullary junction In 2 of 3 cortisone treated animals at 15 days, minimal tubular changes and intact papillae were noted (fig 3) Rat No 3 had more marked changes in all tubules (but not of the degree seen in control animals), and very early papillary necrosis

Because renal vessels were clamped prior to removing the kidney, evaluation of the degree of vascular dilatation and congestion in these sections is difficult

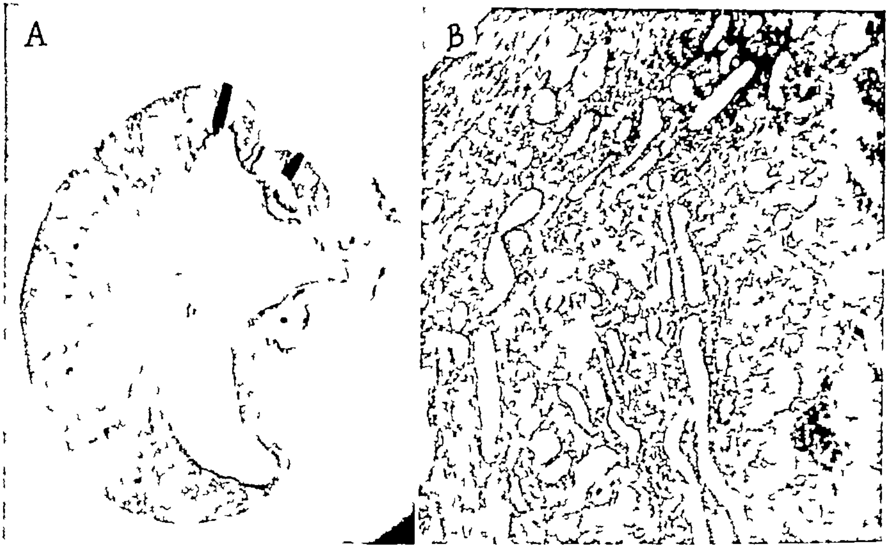

FIG 2 *A*, kidney 15 days after ureteral ligation No cortisone ×8 *B*, same as *A* Note marked dilatation of tubules ×92

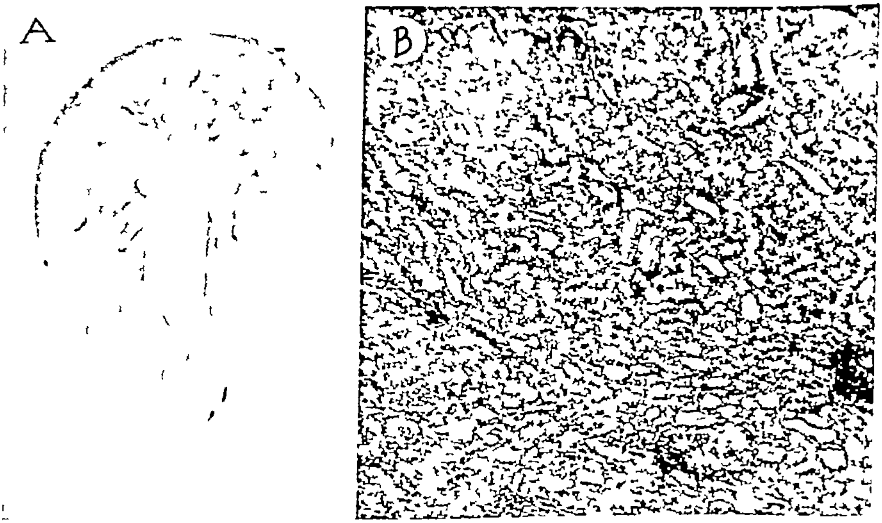

FIG 3 *A*, kidney 15 days after ureteral ligation Cortisone 6 25 mg per day ×8 *B*, same as *A* Note minimal tubular changes ×92

This procedure itself tended to cause apparent congestion of vessels which might be confused with possible hormonal effects No attempt is being made, therefore, to interpret vascular changes noted microscopically in these sections

DISCUSSION

The pathologic changes following acute ligation of the ureter have been described[1] [2] Although the rate at which these changes develop varies somewhat in different animal species, the pattern of events is similar There is accumulation of fluid in the distended pelvis proximal to the ligature followed by a rapid dilatation of renal tubular network As these changes progress over a period of weeks, the kidney is converted to a bag of fluid surrounded by a thin shell of fibrous tissue containing atrophic remnants of nephrons Papillary necrosis and atrophy, particularly in animals with monopyramidal kidneys, is seen early in this sequence of changes Despite obstruction to the flow of urine, the kidney continues to function for a considerable period of time as is seen from increasing amounts of fluid present in the pelvis and changing composition of this fluid in regard to electrolytes, urea, etc[3] The exact mechanisms involved in these changes are not apparent It is known, however, that increasing intrarenal pressure by renal vein occlusion will increase the rate of their development[1]

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[1] Hinman, F Hydronephrosis I The structural changes Surgery, 17 816 1945

[2] Strong, K C Plastic studies in abnormal renal architecture parenchymal alteration in experimental hydronephrosis Arch Path 29 77 1940

The renal weight changes seen in these experiments are similar to those reported by Eranko and Niemi,[4] who, in studying alterations in renal phosphatase activity in rats with hydronephrosis, noted a weight ratio of obstructed to unobstructed kidney of 2 0 or greater in animals examined 12 to 16 days after ureteral ligation These authors described a progressive weight increase in contralateral unobstructed kidneys as the interval between ureteral ligation and sacrifice was prolonged, which was presumed to be due to compensatory hypertrophy

The first observation that hormones could ‘ protect” the hydronephrotic kidney was made by Selye and Friedman[5] in 1941 They demonstrated that female mice given testosterone daily had delay in renal atrophy seen after ureteral ligation These authors noted that macroscopically the hydronephrotic kidneys in animals receiving testosterone “looked better” and were more reddish in color ” This was confirmed in rats by Weinstein, and others[6] who also commented upon the increased vascularity of hydronephrotic kidneys in animals which received testosterone In 1950, Homburger, and others[7] noted a similar protective effect of various androgenic compounds in female mice with ureteral ligation

Although these substances have been shown to inhibit and prevent the changes which occur after ureteral obstruction, the mechanism of this is not known In this regard, it is interesting that both Selye and Friedman, and Weinstein, and others have commented upon vascular changes seen in androgen treated animals Glomerular hyperemia has been described in rats receiving cortisone[8, 9] and since effective filtration pressure within the glomerulus is in part determined by arterial blood pressure, efferent and afferent arteriolar resistances, and renal venous pressure[10] it is possible that hormonal effects on renal vasculature alter this filtration and thus tend to decrease the rate of hydronephrotic changes

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[3] Hinman, F Hydronephrosis II The functional changes Surgery 17 816, 1945

[4] Eranko O and Niemi O Histochemically demonstrable phosphatases in the kidney of hydronephrotic rats Acta Path Microbiol Scand 35 357 1954

[5] Selye H and Friedman S M The beneficial action of testosterone in experimental renal atrophy caused by ligature of the ureter Endocrinol 29 80 1941

[6] Weinstein B B Byrne W H Sustendal G F and Collins C G Effect of testosterone propionate and diethyl stilbestrol on the kidney after ligation of the ureter Urol & Cutan Rev 47 281 1943

Homburger F Forbes I and Desjardins R Renotropic effects of some antrogens upon experimental hydronephrosis and upon the clitoris in the mouse Endocrinology 47 19 1950

[8] Friedman S M Friedman C L and Nakashima, M Action of cortisone on cardiovascular renal effects of desoxycorticosterone acetate Am J Physiol 163 319 1950

[9] Selye H Interactions between the adrenocorticotrophic hormone (ACTH) and the somatotrophic hormone (STH) in respect to their effects upon the kidney and the cardiovascular apparatus Proc 2nd Clin ACTH Conf 1 95 1951

The deleterious effect of hydronephrosis on integrity of renal vessels has been noted [11] This vascular damage, plus increased intrapelvic fluid pressure would tend to cause extravasation of fluid into interstitial tissues In vivo studies have shown that cortisone increases general vascular tone, and suppresses nonspecific inflammatory changes of vascular dilatation, particularly of arterioles, and lessens damage to vascular endothelium as measured by extravasation of fluid and cells [12] [13] This effect of cortisone was seen in the present study by diminished accumulation of interstitial edema in animals receiving cortisone

It has been reported that a decreased food and water intake, accompanied by weight loss, prevented renal hypertrophy associated with nephrectomy [14] Weight loss was rapidly produced in the present experiments by the large dose of cortisone employed, however, it should be noted that "protective" effects of the hormone described in these experiments were not entirely related to body weight changes

SUMMARY

Cortisone protected the kidney from the acute effects of ureteral ligation as evidenced by a smaller, more normal appearing organ, accumulation of less hydronephrotic fluid, and less tubular dilatation on microscopic examination Although compensatory hypertrophy appeared greater in the unobstructed kidneys of control animals than those receiving cortisone, this difference was not statistically significant when these changes were analyzed in terms of body weight

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[10] Smith, H W The Kidney New York Oxford University Press, 1951

[11] Altschul, R and Fedor, S Vascular changes in hydronephrosis Am Heart J , **46** 291, 1953

[12] Zweifach, B W , Shorr, E and Black, M M The influence of the adrenal cortex on behavior of terminal vascular bed Ann New York Acad Sci , **56** 626, 1953

[13] Wyman, L C , Fulton, G P and Shulman, M H Direct observations on the circulation in the hamster cheek pouch in adrenal insufficiency and experimental hypercorticalism Ann New York Acad Sci , **56** 643, 1956

[14] Block, M A , Wakim, K G and Mann, F C Appraisal of certain factors influencing compensatory renal hypertrophy Am J Physiol , **172** 60, 1953

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PERIPELVIC LYMPHATIC RENAL CYSTS

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From the Department of Urology, University of Texas Medical Branch, Galveston, Texas

Cysts of the renal region are fairly frequent in occurrence, relatively obscure as to etiology, and often difficult with regard to classification. Perhaps the simplest grouping is that encompassed by the terms "renal," "pararenal," and "perinephric." Renal cysts, such as the solitary, multiple, and polycystic types, are in need of no categorical summation. The terms "pararenal" and "perinephric," however, are at times confused. Pararenal cysts are best described as being divorced from the renal parenchyma and capsule, yet closely associated with the kidney and its investments in the renal fossa. Perinephric cysts, in contradistinction, lie either within the capsule of the kidney or so closely associated with the capsule that a differentiation cannot be made.

Three types of perinephric cysts occur: 1) between the two layers of the capsule, 2) between the capsule and the parenchyma, and 3) as an ostensibly separate entity stylized as peripelvic lymphatic cyst formation.

Henthorne,[1] in his review of renal cysts, credits Rivolta as being the first to venture the opinion that cysts exclusively confined to the renal hilar region were in many instances actually a residuum of lymphatic ectasia. Henthorne concluded from his study of this type of cyst that in view of their location, because of their relative inseparability from the renal pelvis, and from their tendency to insinuate deeply into the sinus renalis and course along major blood vessels in a fashion suggestive of lymphatic trunks, such cystic structures were quite possibly lymphatic in origin. A review of all the collected cases reveals that no communication between such cysts and the renal pelvis has ever been demonstrated.

The matter of etiological derivation has been reiterated by most workers to revolve about an inflammatory, obstructive hypothesis. These cysts have occurred predominantly in persons past the fifth decade. Associated parenchymal scarring and cortical cyst formation in addition to a clinical history of infection or calculus disease, have been obtained in most instances. That some workers have found the parenchymal lymphatics concomitantly dilated has seemed to add credence to a lymphatic ectatic etiology. More recently Carr[2] and Goodwin[3] have broached the question as to the role of the lymphatics as a collateral drainage system in the presence of infection and obstruction more distally in the urinary tract. Their statement that lymphatic ectasia at the hilus can reach a stage of clinical importance spices conjecture regarding the mechanism of development of this peculiar type of hilar renal cyst.

Recently three patients presenting urographic and anatomic evidence of

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Read at annual meeting of South Central Section of American Urological Association, Mexico City, October 28–November 1, 1956.

[1] Henthorne, J. C.: Peripelvic lymphatic cysts of the kidney. Am. J. Clin. Path., 8: 28, 1938.

[2] Carr, R. J.: A new theory on the formation of renal calculi. Brit. J. Urol., 26: 105, 1954.

[3] Goodwin, Willard: Personal communications.

peripelvic cyst formation corresponding grossly to the description of perinephric lymphatic cysts, were seen at the University Hospital An evaluation of the clinicopathologic findings in these persons seemed warranted to ascertain whether or not any demonstrable relationship to primary lymphatic ectasia could be adduced

CASE REPORTS

W D 9130-M A 70-year-old Negro man was admitted to the University Hospital for treatment of advanced prostatism The urologic evaluation revealed the presence of a very large vesical calculus and a relatively small, obstructive, benign adenomatous hyperplasia Excretory urograms demonstrated a mal rotation of the left kidney and a crescentic deformity of the right renal pelvis, suggestive of a space-occupying lesion in the hilar region of the right kidney (fig 1, *A* and *B*) Since the man's urgent symptoms were related to the obstruction at the vesical neck, the calculus and prostate were removed prior to further investigation of the upper urinary tracts Subsequent to retrograde studies, exploration of the flank was carried out and, upon reaching the kidney, the area of the renal pedicle was immediately cleansed and secured between the fingers of an assistant Further exploration revealed that the mass occupying the hilar region was a peripelvic cyst and the parenchyma was otherwise normal The cystic structure impinged upon the renal pelvis and insinuated deeply into the sinus renalis The cyst wall was markedly adherent to the pelvis and could not be separated The sac was opened and its interior was explored for a possible communication with the renal collecting system, none was found The cyst was then excised, with the exception of that portion adherent to the pelvic wall (fig 1, *C* and *D*)

Pathologic study of the tissue revealed that the sac was composed of fibrous connective tissue and that a few ectatic, endothelially lined vascular spaces, having the morphologic features of veins, were present These vascular spaces did not seem to be an integral part of the mass, but occurred in the adjacent connective tissue

The second patient, a 74-year-old white man (F R 12295-M), was admitted to the University Hospital for investigation of progressive prostatism Excretory urography delineated a normal right kidney, but no function was apparent on the left A left retrograde urogram (fig 2, *A*) demonstrated a rather marked crescentic deformity of the renal pelvis in the region of the hilus, suggestive of a space-occupying lesion, and ostensibly the etiology of the diminished renal function Exploration of the left flank was carried out When the kidney was reached, the vascular pedicle was immediately cleansed and secured between the fingers of an assistant Further exposure revealed that the interior of the kidney had been almost completely replaced by a cystic mass derived apparently from the hilus of the kidney Subsequent to evacuation of the cyst fluid, the renal parenchyma was found to be so attenuated that nephrectomy was deemed advisable (fig 2, *B*, *C*, *D*)

The pathologist's report stated that the renal pyramids were not associated with the cyst, but several smaller cysts lay adjacent to the larger one Micro-

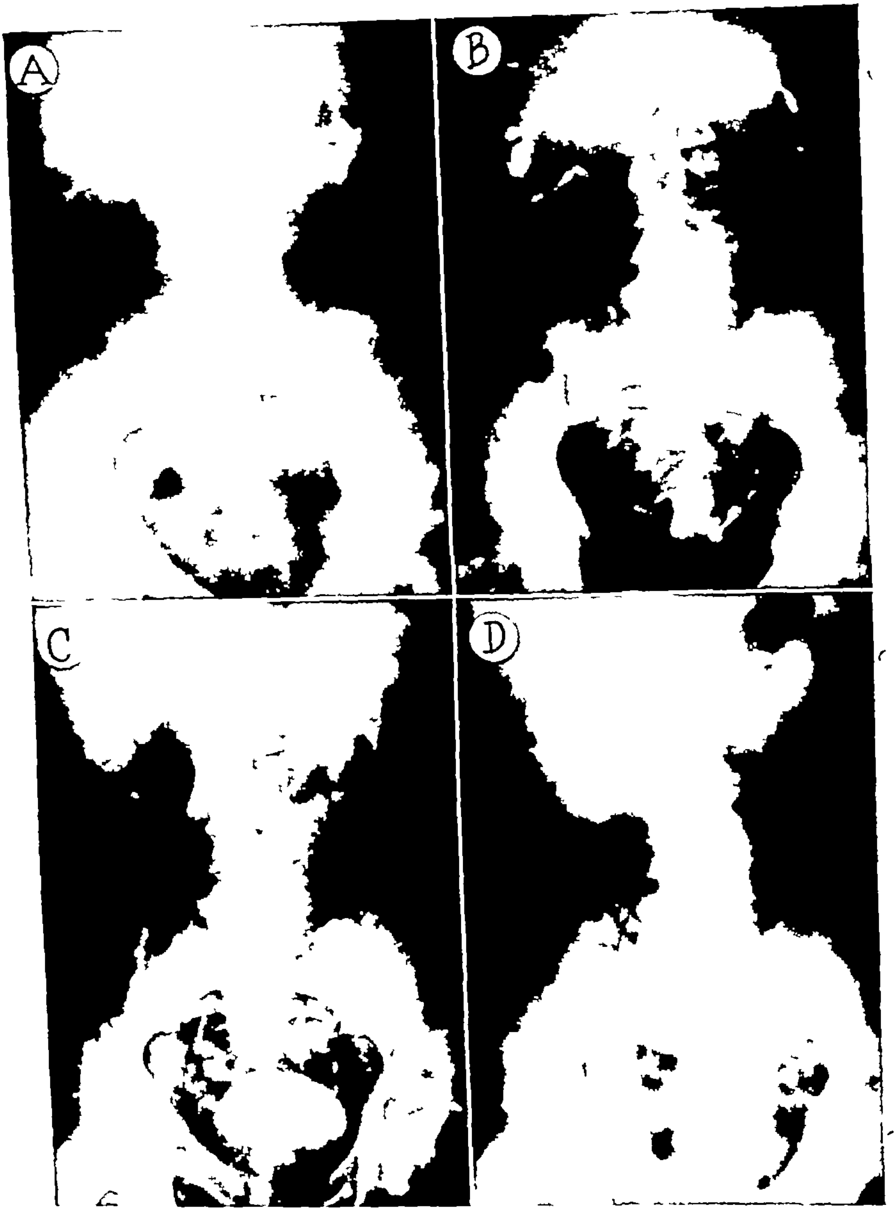

Fig 1 Excretory urograms A, note vesical calculus B, right pelvic deformity outlined C early postoperative film D, later postoperative film

scopic examination of the area surrounding the cyst revealed an extensive chronic inflammatory reaction involving the ureter and the renal pelvis, with an infiltrate predominantly lymphocytic In the peripheral portion of the renal cortex there were many scarred areas with hyalinized tubules, areas of fibrosis, and distortion of adjacent tubules In some areas, occasional dilated venous and lymphatic peripelvic cyst formation corresponding grossly to the description of perinephric lymphatic cysts, were seen at the University Hospital An evaluation of the clinicopathologic findings in these persons seemed warranted to ascertain whether or not any demonstrable relationship to primary lymphatic ectasia could be adduced

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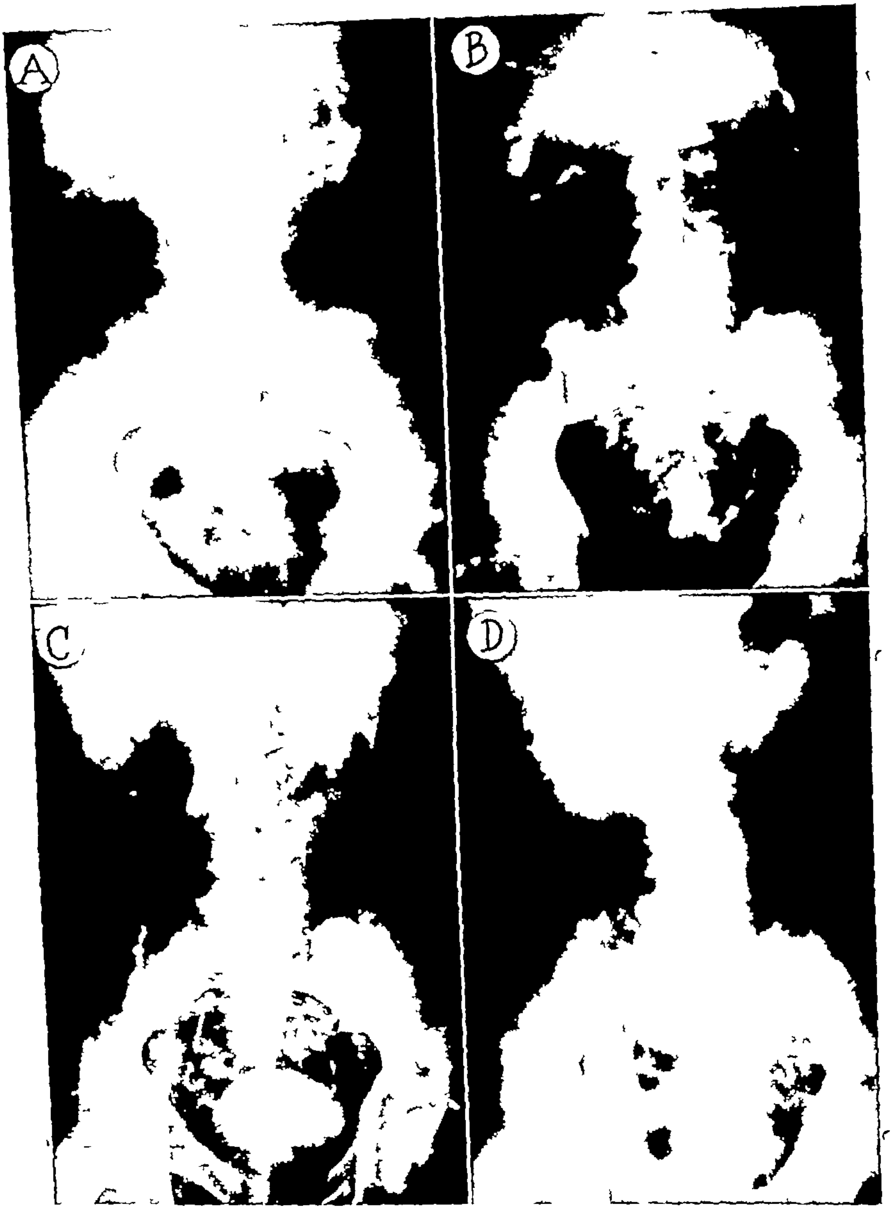

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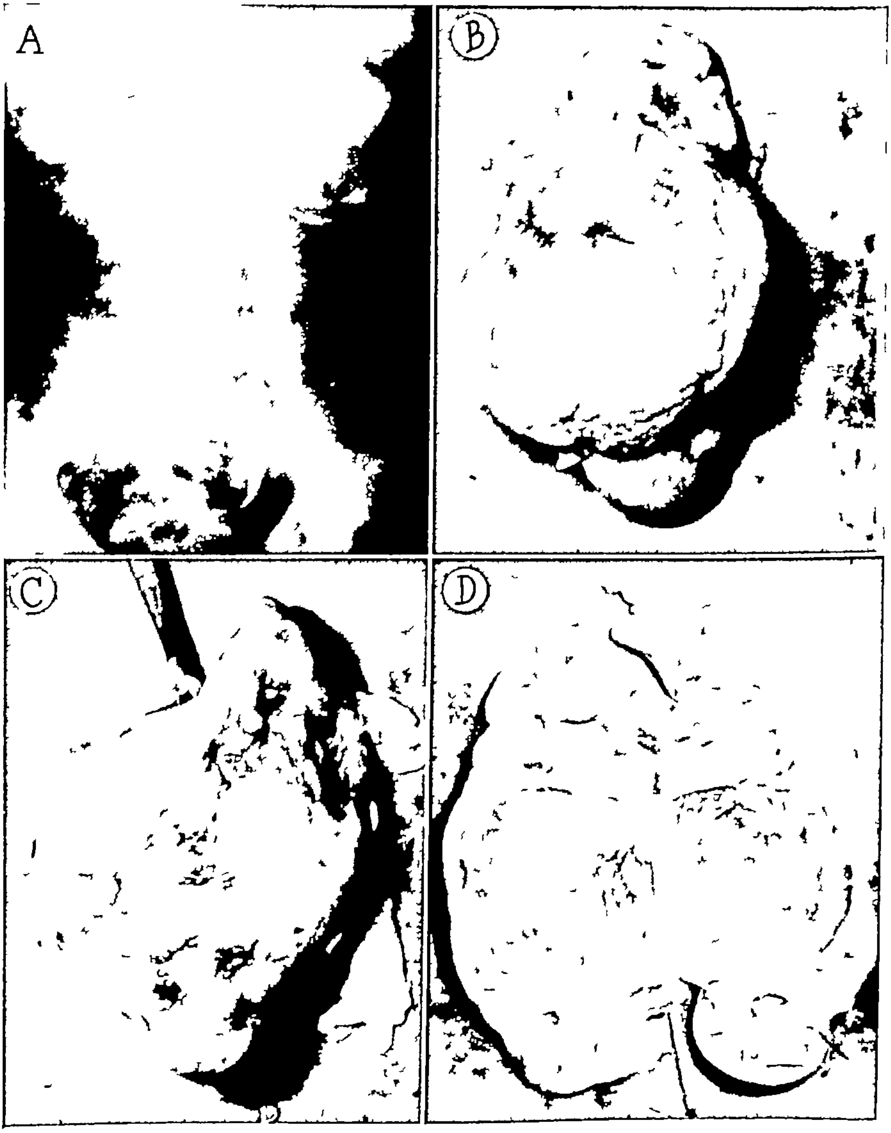

FIG 2 *A*, left retrograde pyelogram with pelvic deformity outlined *B*, view of hilar portion of kidney specimen *C*, view of parenchymal distortion produced by cyst *D*, kidney bisected, size of cyst visualized

channels were noted, but there did not seem to be any connection between these channels and the cyst wall The sac wall was composed of dense fibrous tissue No communication could be discerned between the cyst and the renal pelvis or any portion of the collecting system, and no definite derivation from intrarenal or intraparenchymal structures could be ascertained

The third patient, a 48-year-old Negro woman (R H 12458-M), was seen in the outpatient clinics of the University Hospital for evaluation referable to many previous attacks of cystitis In the course of study, an excretory urogram

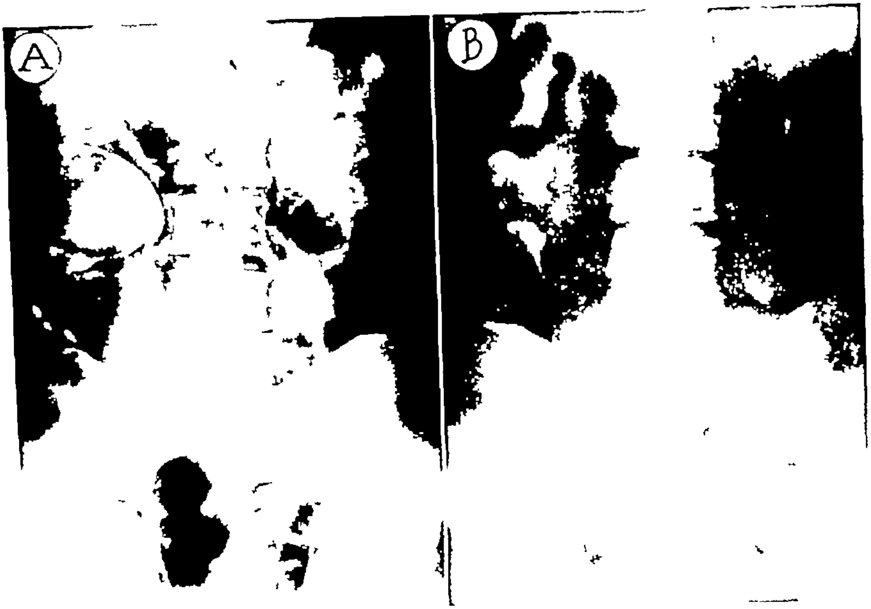

FIG 3 Excretory urograms *A*, with right renal pelvic deformity visualized *B*, postoperative appearance of right kidney

delineated a deformity in the hilar region of the right kidney (fig 3, *A*) A smooth, crescentic deflection of the renal pelvis was outlined, signifying the presence of a space-occupying mass at the hilum Retrograde urograms were confirmatory There had been no symptomatology referable to the upper urinary tracts Gynecologic consultation revealed what ostensibly were the residua of chronic pelvic inflammatory disease Renal exploration was undertaken When the kidney was reached, the renal pedicle was immediately defined, cleansed, and controlled between the fingers of an assistant With further exposure, it could be seen that a cystic structure occupied the hilus of the kidney and delved deeply into the sinus renalis No inflammatory reaction was apparent in the surrounding tissues It was noted that the cystic structure was markedly adherent to the renal pelvis and, in an attempt to dissect it from the pelvis, a tear was made through the greatly attenuated pelvic wall The portion of the pelvis in contact with the cyst was most friable and, in removing the cyst sac, a rather large segment of the pelvic wall was lost Since it was not feasible to reunite the upper and lower margins of the pelvis, in view of the distortion which would have been produced, a portion of the renal capsule was dissected from the parenchyma and turned down over the defect and sutured to the pelvic margin A small nephrostomy tube was utilized to minimize seepage The patient's postoperative course was smooth and, following the removal of the nephrostomy, she continued to do well

Pathologic examination of the excised tissues revealed that the wall of the cyst was composed of dense fibrous tissue and that the portion of the renal pelvis, which was adherent to the cyst wall, demonstrated a chronic inflammatory reaction with an infiltrate predominantly lymphocytic Again, a few ectatic, endothelially lined vascular spaces were noted in sections of the cyst and pelvis, these had the morphologic features of veins Followup urograms (fig 3, *B*) revealed that the kidney functioned well, but that there remained some dilatation of the calyceal system, however, the patient has remained asymptomatic

DISCUSSION

In a review of these three cases from an etiological point of view, *no definite* evidence can be derived from the pathologist's examination to reinforce a contention that lymphatic ectasia had been productive of cyst formation The pathologist who evaluated the material postulated that the presence of an occasional dilated lymphatic space can hardly prove or disprove that such a cyst arose from the lymphatic channels It seemed to him a more likely deduction that the changes visualized in the lymph channels were, in all probability, secondary to the presence of the cyst rather than as a primary pathologic change from which a cyst arose

However, the gross anatomic findings in each of these cases certainly adhere to the accepted description of peripelvic lymphatic cysts which places the location of the cystic structure at the hilus with insinuations deep into the sinus renalis Again, the adherence of the cyst wall to the pelvis is a feature which has been described as characteristic Lymphangiectasis, which has been reported as ostensibly associated with peripelvic lymphatic cysts, was searched for in the other common locations of the body and in these three patients could not be found Reputedly, it exists in 25 per cent of cases

From a perusal of the history in each of these cases, it is noted that the infection and obstruction postulated as etiological by most of the other workers are clearly fulfilled in these three instances Yet it appears that, if an inflammatory hypothesis for the development of such a lymphatic ectasia were reasonable, the collateral lymphatic channels of the capsule ordinarily would adequately compensate for any such obstruction, and thus the theories of Scholl[4] that such peripelvic cysts may arise from remnants of the wolffian body have begun to seem more tenable

A manner in which more conclusive findings could be derived regarding the etiology of these cysts might be in the utilization of the technique of the percutaneous antegrade urogram In the future, our diagnostic plans in these instances will include needle tapping of the cyst with subsequent injection of a combination of one of the urographic media and India ink particles We should thus be able to outline the exact extent of the cystic intrusion into the sinus renalis, to evaluate the absorption of the urographic medium from the cyst, and subsequently at operation (by examination of not only the resected cyst, but also of contiguous perihilar structures) ascertain whether lymphatic connections actually do exist In instances where nephrectomy may be indicated, the entire specimen will be available for evaluation of possible communications and drainage systems

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[4] Scholl, A J Peripelvic lymphatic cysts of the kidney J A M A 136 4, 1948

It would seem that peripelvic cysts, if not a definite entity in respect to etiology, be the genesis lymphatic or not with respect to the urographic changes which they engender, should be considered as a group In reviewing the x-ray appearance of the recorded cases of such cysts, we find that the markedly repetitive similarity of each, with respect to the pelvic deformity produced, is striking It could almost be promulgated that, in any instance of deformity of the renal pelvis wherein a smooth, crescentic, medial displacement of the pelvis occurs, specifically in the hilar region, this finding should engender the diagnosis of peripelvic cyst

It is, of course, redundant to mandate that exploration be undertaken in every instance Exploration is necessary for three reasons 1) extirpation of the pressure-producing cyst, removal of the obstruction, and the conservation of functioning renal tissue, 2) to investigate the possibility of parenchymal neoplasm, and 3) to rule out the occurrence of a neoplasm within such a cyst This has not been reported previously, but ostensibly it could occur Of utmost importance, however, is as careful a preoperative diagnosis as possible in order to make certain that an otherwise normal cyst-bearing kidney is not subjected to peremptory nephrectomy At the time of surgery, the immediate securing of the renal pedicle by digital compression or rubber shod clamp will allow a more complete and competent exposure of the kidney, in order to ascertain whether it is salvageable, without the risk of tumor embolization, should such be present It is obvious in instances where the urograms suggest peripelvic cyst that careful cleansing and complete definition of the entire hilus are essential in order to prevent needless sacrificing of such kidneys by immediate pedicle ligation As was seen in one of these patients, peripelvic cysts may so insinuate themselves onto the sinus renalis that their cystic nature may not be apparent until the last vestige of connective tissue has been removed Additionally, often the sole satisfactory surgical adjunct to the preoperative functional evaluation of the kidney is the palpation of the parenchyma itself and this constitutes further inducement for cyst definition and excision prior to arrival at a decision regarding the necessity for nephrectomy

In most instances, resection of the exposed sac wall is sufficient to obviate the deleterious compressive effects of the cyst and no reaccumulation of fluid should occur Should rents be made in the pelvis during the hilar-cleansing period or during circumcision of excess tissue, the renal capsule in the hilar region can be utilized to repair such defects as may have occurred

In conclusion, it bears reiteration that the pyelographic appearance so characteristic of peripelvic cysts should be more often construed as indicative of this rather definite clinical lesion and that more care should be afforded them diagnostically, as well as in their eventual disposition

SUMMARY

Renal, pararenal, and perinephric cyst formation has been differentiated

The postulation that hilar peripelvic perinephric cysts are the results of lymphatic ectasia is discussed, and the characteristic clinical features are described

Material derived from three patients exhibiting urographic and anatomic qualifications for consideration as instances of perinephric lymphatic cyst is evaluated No conclusive evidence ascribing lymphatic ectasia as etiological could be ascertained

A method for the further investigation of this type of cyst, via percutaneous injection, is advanced

The necessity for more careful preoperative and surgical investigation is urged in reference to conservation of salvageable renal tissue

The need for greater dissemination of the specificity of the urographic appearance of peripelvic cyst formation is expounded

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CHYLURIC SYNDROME (PYELOLYMPHATIC REFLUX?)

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Chyluria is the name given to the mixture of chyle and urine, which takes a milky-white color because of presence of dispersed or emulsified fat coming from the renal or periureteral lymph vessels Therefore, urine in this syndrome contains all the lymph elements, among which albumin, fat and fibrin are easy to detect Occasionally, urine passed is so thick that, if allowed to stand for a while, separation of a superficial layer of caseous matter becomes apparent

The origin of the lymphatic obstruction which causes this syndrome may be either parasitic or mechanical, it results in the establishment of a fistulous communication of the lymphatic vessels which empty their contents into the urinary tract So far, it has not been possible to determine the exact place where this communication occurs

Chyluria may at first sight be mistaken for phosphaturia, intense pyuria or lipuria Microscopic and chemical differentiation is usually easy to accomplish in such cases Physical and chemical tests added to examination of the urinary sediment definitely permit establishing a correct diagnosis Fatty drops as well as lack of fibrin are typical signs of lipuria, this syndrome occurs in patients suffering from diabetes or in those intoxicated with phosphorus Existence of pyuria is determined through microscopic examination Hyperdensity of the urine is an evident sign of chyluria

Nonparasitic chyluria may appear in different processes—traumatic, abdominal or pelvic lesions—which result in the rupture of lymph vessels pertaining to the urinary tract or located nearby, this may occur during pregnancy and labor periods as well as in certain forms of neoplasia, tuberculosis, cysts or ganglions located in the renal hilum and in the ureter Magnus Levy and others have ascertained the presence of chyle in the urine of some diabetic patients, while Mohr has reported a case of chyluria in an 8-year-old child suffering from diphtheria Le Dantec has found several cases of tuberculous peritonitis accompanied by chyluria, while Vogelius has reported one in which several diseases were associated Cases where different traumatisms coincide with chyluria are infrequent So far, only three of such cases have been reported in medical literature those published by Hunt, Ciaury, and Lazarus and Marks

Prior to Pecquet's description of lymphatic circulation, different hypotheses had been set forth in an attempt to explain the cause of chyluria, but it was Morgagni who associated this affection with lymph circulation disorders In 1869, Wucherer proved the existence of filariae in certain cases of chyluria

Parasitic chyluria is due to an infection caused by a nematoid, chiefly the Wuchereria bancrofti filaria Although this disease is usually transmitted by a mosquito of the "culex" type, there are other species also capable of transmitting it The infectious process is quite comparable with that of malaria, i e , the mos-

Accepted for publication November 1, 1956

quito sucks the blood from a person suffering the disease, which blood contains filaria embryos in circulation These embryos will have developed into larvae two or three weeks after they have been inoculated by the mosquito It is through the latter's bite that the disease is transmitted Due to their short number, filaria embryos are not easily found in the patient's blood until nine months after inoculation Time of appearance of the first symptoms may range from one month to several years

Transmission period begins with the presence of large numbers of microfilaria in the blood, development of the larvae in the mosquito is completed within a period of 14 to 21 days Located in the head or in the proboscis of the insect, it is from these places that they are inoculated, thus transmitting the disease

In its early stage, human filariasis is generally characterized by lymphadenitis and lymphangitis—particularly in spermatic cords, lower limbs and scrotum—accompanied by fever and lethargy If repeatedly bitten by parasite-vector mosquitoes, the patient passes to the chronic stage in which chyluria or different phenomena (elephantiasis, etc) may appear Occasionally, not until two or three years after inoculation are parasite embryos found in the patient's blood However, once their presence has been determined, it can be checked as many times as necessary during the illness Not before 9 months from time of their penetration into the circulatory system are microfilariae likely to be discovered in smear or in thick drop The best time for taking and examining the blood is between 10 00 p m and 2 00 a m

Prophylactic measures are similar to those taken in the fight against malaria, with the difference that there are no curative or preventive treatments efficient enough for filariasis Tropical or subtropical countries are the most affected by this disease

Interesting experiences on the subject have been published by Barnes, Kawaichi, Abeshouse, and Kutzmann Wood, Wakefield and Thompson, and A and E de la Peña have also written particularly remarkable papers on pyelo lymphatic reflux as mechanism of chyluria

Our case clearly evidences the radiographic injection of the thick renal lymphatics

Wesson assumes that chyluria is due to obstruction of the thoracic duct as a result of inadequate collateral lymph-circulation as well as rupture of the intrarenal vessels Alike this author, we have confirmed the phenomenon of the passage to the lymphatics on performing the first retrograde pyelography (fig 1)

So far, the number of reliably confirmed cases of interlymphatic-urinary communication through the renal parenchyma as a result of chyluria has been very short (less than 7)

All this would appear to have nullified the hypothesis which tried to establish a relationship between the chyluric syndrome and the passage of lymph through the glomeruli At present, there is a widespread belief that this syndrome is due to a fistulous intraparenchymatous communication resulting from the rupture of swollen vessels (Marion, Ponfick, Stejskal, Port, Pope, Bloch, etc)

In 1863, Ackermann associated chyluria with obstructive mechanic disturb-

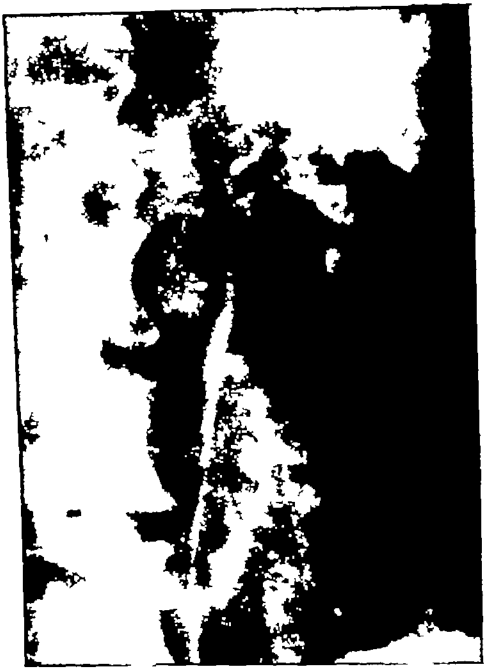

FIG 1 Retrograde left pyelogram Reflux from the calyces toward the renal hilum can be observed

ances of the lymphatics producing ecstasy as well as valvular insufficiency of the system In filariasis, obstruction of the thoracic duct is caused by nematodes, even after these have disappeared obliteration might persist (Manson)

Hampton accepts the hypothesis which explains lymphatic ecstasy and passage of lymph into the urinary system as due to the great fragility of unsound renal lymphatics In the course of an autopsy carried out on a person who had been suffering from chyluria, MacKenzie found the thoracic duct obstructed and thereby inferred that the passage of lymph into the urine was caused by that mechanism

To attribute chyluria to other causes, in the case of patients who do not present hematozoaries in blood or in urine but who have been residing in tropical countries, is a fact which many authors have refused to accept

Renal chyluria may be either bilateral or unilateral (as in our case) It may appear and disappear spontaneously, or else be of an intermittent type In some cases, the presence of chyle increases while the person is standing, in others, this phenomenon only occurs in the recumbent position This is attributed to obliteration of the fistula coinciding with a determined position of the body Although the disease in itself is not serious and in some cases it disappears spontaneously, the patients usually die of weakness, anemia and cachexia

There are cases in which the disease has been present for 19, 20 and even 55 years, without any alteration in the patient's general state of health

Different treatments have been suggested, but the various medications employed, i e , sodium citrate, ammonium chloride, vitamins, fuadine, neostibosan, etc , have all proved to be of little curative value

A diet containing little fat, washing of the pelvis with astringents, iodine compounds and silver nitrate are among the curative methods most strongly recommended Some authors have suggested the radical treatment (nephrectomy) for unilateral processes However, this procedure is quite refutable if we consider the general nature of the process In 1945 Julio E Colon, of Puerto Rico, succeeded in curing 2 patients by means of renal decapsulation, after having tried other general and local methods unsuccessfully Antibiotics and chemotherapic treatment are advised in order to prevent associated infections Moreover, some authors agree in considerng this process as of septic nature and therefore antibiotic therapy is indicated In 1947 Stevenson, Gonzalez and Hewitt introduced hetrazan as a specific treatment and proved its low toxicity and usefulness Its chemical composition is 1-dyethylcarbamyl-4-methylpiperazine

CASE REPORT

Mr S L E , *about 50 years old, married, without any pathological antecedent*, was sent to us by Dr Giraldi, of Gibraltar, for examination and treatment In December 1947, the patient had been passing milky-white urine for 6 months, without any other special symptom The patient gave no history of trauma He resided in Jamaica during the last World War General physical examination was negative Urine passed spontaneously during the examination was milky-yellow and turbid

Urinalysis A large number of lymphocytes as well as some leukocytes were found in the sediment No casts, germs or microfilariae were found No Koch bacilli were found in the sediment, though a large number of white cells were discovered Other germs were absent Research for microfilariae in blood also proved negative

Blood Chemical analysis (urea, xanthoproteics, sugar, etc) normal Negative sero-lues reactions Morphological analysis 4,200,000 red cells with 90 per cent hemoglobin The number of leukocytes was practically normal Count Moderate leukopenia, 3,600 Coagulation time and sedimentation rate normal Repeated thick-drop research for microfilariae No microfilaria or embryo appeared to be present

Plain radiograph of the urinary organs Rather large image of left kidney No opaque calculus was seen An intravenous urogram, after having injected uroselectan B in vein, revealed excellent elimination with good filling, normal aspect of calyces and pelvis A cystogram showed no alteration whatsoever of the outline

Considering the negative radiologic examination, a cystoscopy was performed with separation of urines and retrograde pyelography In the bladder, a slight inflammation of the trigone was observed The right ureteral orifice was found to be normal and easy to visualize, with regular flowing of clear, transparent urine The left ureteral orifice was seen to eliminate typical chyluric urine which blurred visuality during the cystoscopic examination and rendered catheterization more difficult to perform on this side Finally, the latter was made possible by means of constant irrigation

Ureteral dynamoscopy with indigo carmine showed results on both sides Colored urine was obtained 4 minutes after the product had been injected intravenously

Once the exploration had been completed and the urine had been separated for analysis retrograde pyelography was obtained after gentle and slow injection of the contrast substance The pyelographic image was found to be normal on the right side On the left side (fig 1), a pyelolymphatic reflux was observed which would appear to indicate the existence of a communication between some renal lymphatics and the urinary tract, in the middle of the left renal parenchyma, whereby the passage of lymph and its incorporation to the urine coming from the kidney would be explained

The progress hence made by the patient was really surprising, since only 48 hours later (during which time the urine appeared somewhat turbid as a result of the blood contained in it) the emictions had been rendered completely transparent, a fact which had previously been observed by Wood

Further analyses showed complete absence of microfilariae, both in blood and in urinary sediment Blood used for these analyses had been taken sometimes during the day and sometimes during the night In the days following the clarification of the urine, the count of leukocytes in blood began to increase until they reached the normal figure

With the patient's consent a further retrograde pyelography of the left side was accomplished for the purpose of checking the condition of the kidney In spite of our having increased the pressure on the contrast injection this second time, no image whatsoever of pyelolymphatic reflux could be determined This catheterization was also used for washing the pelvis with a silver nitrate solution, a procedure which several authors have found successful

Five days later the patient was discharged, not without first recommending to him that he have his blood and urine periodically tested for microfilariae and, should chyluria happen to make its appearance again, to have left ureteral catheterization repeated as well as instillations of a 10 per cent, 20 per cent or 25 per cent solution of sodium iodide through the ureteral catheter

This patient, 8 years after his previous examination in our clinic, voids clear urine during short intervals only, and at present time he is perfectly healthy, in spite of the chronic chyle loss

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THORACIC KIDNEY CASE REPORTS

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AND

VINCENT VERMOOTEN

From the Division of Urology, University of Texas, Southwestern Medical School, Dallas, Texas

Although various types of renal ectopia are fairly common, the finding of an intrathoracic kidney is decidedly unusual Robbins and Lich found ten such instances in the literature and added a case of their own In a review of 13,000 autopsies Spillane and Prather discovered only one intrathoracic kidney

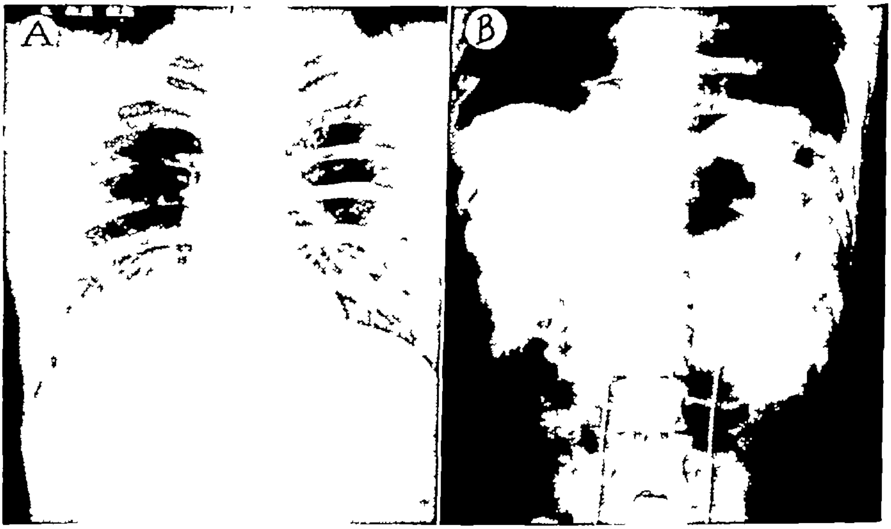

FIG 1

Since the thoracic kidney may be mistaken for a space-occupying lesion originating above the diaphragm, it is of clinical and diagnostic importance to the thoracic surgeon Our case 1 in which the renal nature of an unexplained thoracic mass was discovered only at surgery emphasizes the point

CASE REPORTS

Case 1 A 26-year-old soldier was admitted to the Brooke Army Hospital in July 1945, because of "a round mass in the posterior inferior portion of the right lung field" discovered on routine chest x-ray (fig 1, *A*) The patient seemed well in every respect and the physical examination was not unusual A gastrointestinal series excluded diaphragmatic hernia The preoperative diagnosis was "intrapulmonary tumor, most likely multilocular cyst " On August 21, 1945, a right thoracotomy was performed through the bed of the seventh rib When the

Read by Dr Barloon at a meeting of the Los Angeles Urologic Society January 8 1957 pleural cavity was entered, a mass was encountered immediately above the diaphragm extending medially to the region of the pulmonary ligament, and partially covered by the thinned out diaphragm After dividing the central tendon it became apparent that the tumor consisted of normal right adrenal and kidney The chest was closed

Postoperative excretory urograms and retrograde pyelograms verified the diagnosis of intrathoracic kidney, right (fig 1, *B*)

Case 2 A 25-year-old Korean soldier was seen at the ROKA 1st Hospital in May 1954 complaining of shortness of breath on exertion A roentgenogram of

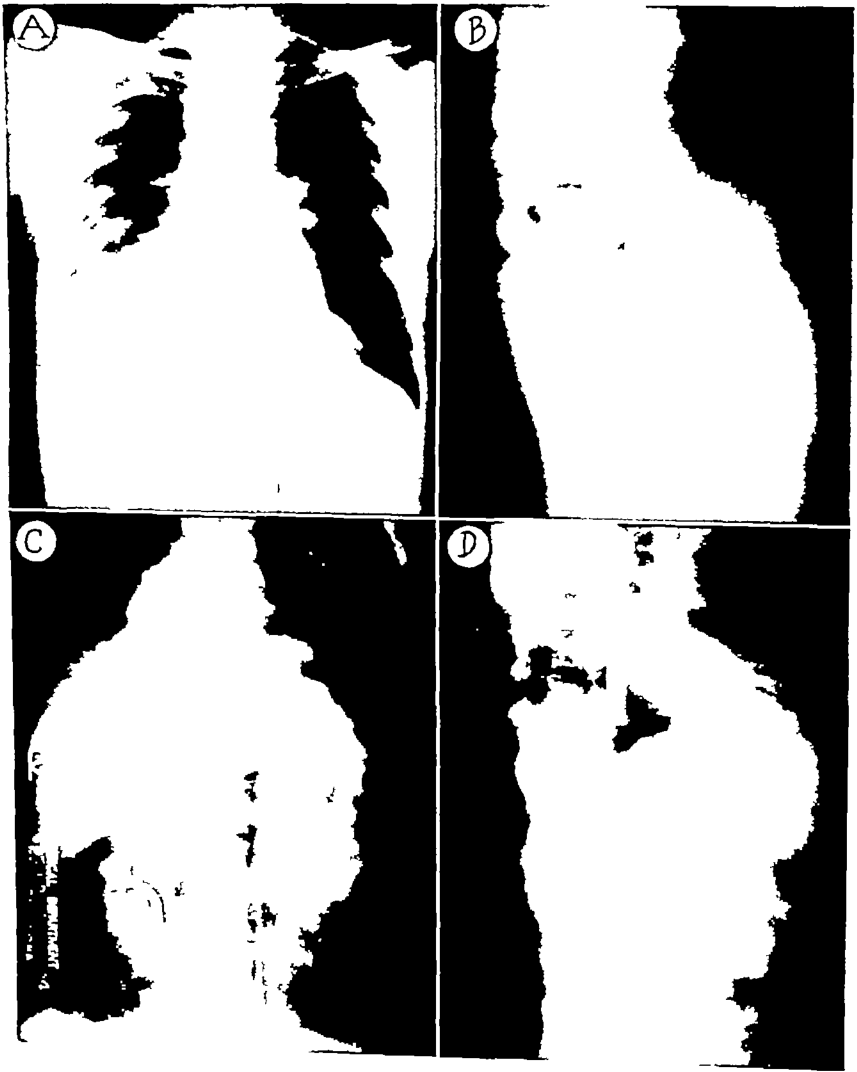

Fig 2

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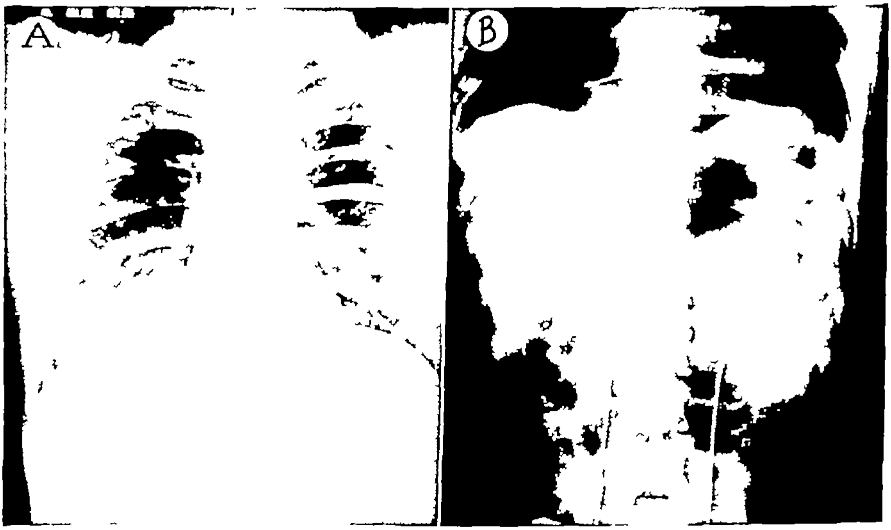

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PRESSURE STUDIES IN THE HUMAN URETER AND RENAL PELVIS

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The urologist is frequently confronted with problems of hydronephrosis hydroureter, ureterovesical reflux and other dysfunctions of the renal pelvis and ureter The purpose of this communication is to report the basal pressure frequency and amplitude as well as duration of peristalsis in the renal pelvis and ureter Several methods have been used in the study of the motor physiology of the ureter These include direct observation of the isolated intact ureter,[1] cystoscopic evaluation of rate and force of ureteral peristalsis,[2, 3] direct observation of the exteriorized trigone,[4] measurement of the action potentials of isolated intact ureteral segments,[5, 8] cinefluoroscopy,[9] and pressure measurements by means of a hydrophorometer [10, 14] None of these techniques recorded absolute pressure values, most of them required subject of interpretation of the measurements In addition many of them introduced an error as a result of a large foreign body such as a balloon or cannula As Finkle[15] points out, there is a great deal of discrepancy in the literature regarding both terms and results in measuring ureteral peristalsis The use of an open end 4F ureteral catheter connected to a sensitive external recording device, as in the experiments recorded below, eliminates the error due to the presence of a large object such as a balloon in which pressure in the viscus is being recorded A similar technique has been used in recording cardiac and gastrointestinal intraluminal pressures [16, 17]

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* Damon Runyon Research Fellow

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the chest revealed infiltration of the right lung, presumed to be tuberculous There was also a mass protruding above the left diaphragm (fig 2, *A* and *B*) Its shape and position suggested the possibility that it was the upper half of the left kidney An intravenous urogram and retrograde pyelography confirmed this impression (fig 2, *C* and *D*) No surgical treatment was indicated

DISCUSSION

The permanent kidney arises in the pelvis at the level of the twenty-eighth somite (fourth lumbar vertebra) and ascends to its normal position Faulty development of the pleuroperitoneal membrane may result in the foramen of Bochdalek in the posterior leaf of the diaphragm In the presence of this defect the kidney has an opportunity to migrate upward into the chest

One may assume that traumatic rupture of the diaphragm could result in cephalad migration of the kidney if high vascular derivation is present

A renal mass presenting in the lower chest on roentgen examination must be differentiated from neurofibroma, pericardial cyst, and diaphragmatic tumor

SUMMARY AND CONCLUSIONS

Thoracic kidneys are rare When present they may present a diagnostic dilemma if they are mistaken for other intrathoracic space-occupying lesions Pyelography clarifies the issue

Two cases of this condition are reported briefly

Intrathoracic kidney must be differentiated from other supradiaphragmatic masses A diagnosis is established by excretory or retrograde urography

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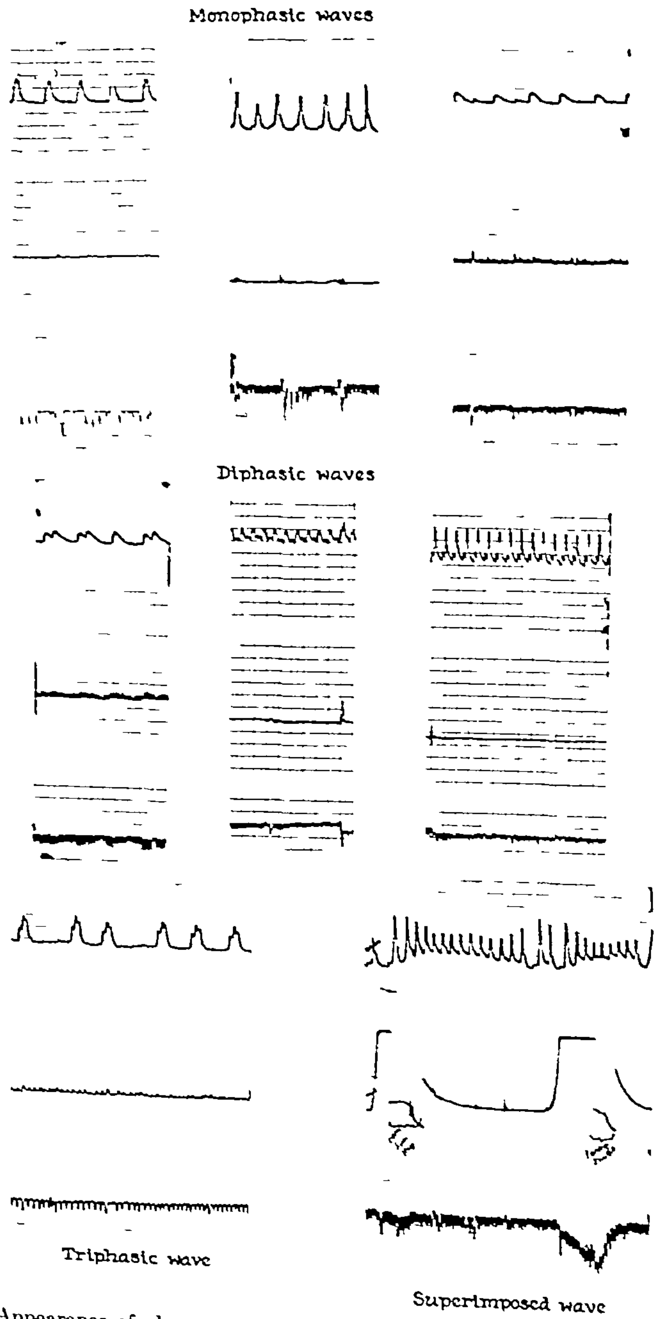

Monophasic waves

Diphasic waves

Triphasic wave

Superimposed wave

FIG 1 Appearance of phasic waves in renal pelvis and ureter as recorded through an open lumened catheter Simultaneous ureteral (top) bladder (middle), and pneumographic (lower) pressure recordings Amplitude One mm equal to 1 cm water pressure except where indicated in lower right record Speed 0.25 mm per second (3 large squares per minute) except in upper and lower left records, where six large squares represent 1 minute

METHOD

Observations were made on 17 adult females with apparently normally functioning urinary tracts. Each of the subjects had a normal intravenous urogram and a normal value for blood urea nitrogen. A 4F ureteral catheter was passed to the renal pelvis. A 20F Foley was inserted into the bladder. Both catheters were connected to Statham P-23B electrical transducers, the system was filled with water, pressures were recorded by means of a Sanborn poly-viso recorder equipped with strain gauge amplifiers. A pneumograph was tied to the chest for the purpose of measuring respiratory and body movement. After noting pressures in the renal pelvis, the recordings were made at the level of the midureter by withdrawing the tip of the catheter 7 to 9 cm. The catheter was then withdrawn an additional 8 to 10 cm. and a recording made in the lower third of the ureter. A 20 to 30 minute tracing was taken at each of the three sites. Patency of the recording system was assured by periodically lifting the head, straining, and deep breathing. The subjects received no premedication or anesthesia. The pH and the volume of the urine excreted during the period of the pressure measurements were noted.

RESULTS

A. *Basal pressure.* The basal pressures remained constant throughout the periods of observation in the individual subjects. They averaged 14.7 cm. of water in the renal pelvis, 13.5 cm. in the midureter and 13 cm. in the lower third of the ureter. Two subjects complained of continuous colicky abdominal and back pain during the pressure measurements. In these patients the basal pressures

TABLE 1. *Intraluminal pressure (cm. of water) and amplitude (cm. of water), frequency (per min.) and duration (secs.) of superimposed phasic pressure waves in urinary tracts of 17 normal women*

Case	Renal Pelvis				Mid ureter				Lower Third of the Ureter			
	Basal pressure	Phasic waves			Basal pressure	Phasic waves			Basal pressure	Phasic waves		
		Freq	Amp	Dur		Freq	Amp	Dur		Freq	Amp	Dur
1					70*	3	5–7	4–16				
2	9	3	2	4–12	12	1	3	6–14				
3	24	7	5	8	21	7	5	8	21	7	12	8
4	25	5	5	12	27	4	5	12–15	10	6	3	10
5	16	1	3	6–16	14	1	3	4–16				
6	6	4–5	3	4–10	5	4–5	2	6–12	6	4	4	4–10
7	14	5–7	4–6	8								
8	22	3	2	16	22	4	4	16	22	2–3	13	10
9	15	3	6	10	13	2	8	10	13	2	13	13
10	8	8	2	7	8	4–5	2	12	6	4	4	6
11	8	6	6	10	8	5	4	6	8	3–9	10–25	10
12	13	5–6	1	10	47*	8	2–3	6–7				
13	20	3–4	3	6	19	2–4	4	12–20				
14	13	5–6	4	6	12	2–4	3–12	8–16				
15	13	1–2	11	10	13	1–2	10–12	12–16				
16	14	1–3	2	4	15	2	6	8	15	1	6–16	10
17	15	1–3	4	8	15	1–2	7	8	15	1–3	7	8

* Continuous pain during recording.

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EARLY DELIGATION OF THE URETER

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Accidental ligation is the most common injury to the ureter during pelvic surgery. The principle of deligation has been condemned and discarded in the past by many authors but in the light of our recent experience, we strongly believe that deligation should be revived. This calls for close co-operation between the surgeon reopening the abdomen from above and the urologist manipulating the ureteral catheter through the cystoscope from below at the same time. During the past 19 months we have deligated 5 consecutive, unselected cases of unilateral injured ureters. The time interval between injury and surgical deligation varied from 5 to 33 days. The results have been uniformly excellent and we believe that they are worth reporting.

INTRODUCTION

Injury of the ureter is a surgical complication which is far more common than is generally assumed. Statistics vary from 10 per cent in radical hysterectomies or difficult pelvic surgery to 0.5 per cent in routine "easy" hysterectomies. A number of unilateral ligations which occur during the course of pelvic surgery are not recognized and remain asymptomatic with ultimate silent autonephrectomy of the involved side. Since there is a tendency to report the successful repair of ureteral injuries, rather than all instances of accidental injuries of the ureter, the statistics are obviously misleading. In addition, a certain number of ligated ureters spontaneously deligate themselves either by the dissolution of the catgut suture or by reanastomosis due to increased intraureteral pressure. The types of injuries in order of frequency, have been reported as: 1) ligation, 2) kinking by ligature, 3) division, 4) partial laceration, 5) crushing by clamp, and 6) necrosis secondary to contusion or stripping of the blood supply. If the injury is detected during surgery, the recommended treatment has varied from ureteroureteral anastomosis or ureteroneocystostomy with or without splints to ureterosigmoidostomy, permanent ureteral ligation or cutaneous ureterostomy. If the ureteral injury is detected following surgery, the accepted treatment has been preliminary diversion of the urinary tract, usually by nephrostomy, followed by reconstructive surgery of the lower ureter at a later date. Early deligation has been advocated by only a few. However, we believe that early deligation is the treatment of choice for ureteral injuries if the condition of the patient warrants definitive therapy.

DIAGNOSIS OF URETERAL LIGATION

The symptoms from ureteral ligation depend on whether the injury is unilateral or bilateral, whether occlusion is complete or incomplete, whether there is leakage of urine into the peritoneal cavity or to the outside, and finally whether or not

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Read at annual meeting of South Central Section of American Urological Association, Mexico City, October 28–November 1, 1956.

were 70 to 40 cm of water These values are not included in the computation of average basal pressure (table 1)

B *Character and amplitude* The peristaltic waves usually showed definite rhymicity Occasionally couplets and triplets were noted and were followed by a refractory period In general, four different wave types were noted Monophasic waves occurred most frequently Diphasic waves also were noted These occurred in all parts of the urinary tract and appeared either as a small undulation superimposed on the ascending or descending limb of the wave Triphasic waves were noted in two subjects A slow, undulating wave upon which monophasic spikes were superimposed occurred in the lower third of the ureter in one patient during a voiding contraction of the bladder (fig 1) Maximal pressures averaged 4 cm above the base line in the midureter, and 8 9 cm in the lower third of the ureter

C *Volume and pH* The volume of urine excreted during the recording period varied from 60 to 365 cubic centimeters There was no correlation between the urine excreted per minute and the level of the basal pressures, the amplitude of the peristalic waves or the frequency of the waves The pH of the urine varied from 6 0 to 7 0 There was no apparent relationship between pH and pressure values

DISCUSSION

Factors which influence the basal pressure and phasic wave and peristalic activities include not only the inherent tone of the urinary tract smooth muscle coats but also the position of adjacent viscera, the intra-abdominal pressure and the volume of urine which is presented to each segment of the urinary tract The complex interplay of factors which produce ureteral and renal pelvic pressures has not yet been solved It appears from our study that there is a relatively constant basal pressure in all parts of the urinary tract in a given individual The basal pressure values are similar to those found in intraluminal pressure measurements in the gastrointestinal tract suggesting that the factors which produce it may be the same for intra- and extraperitoneal hollow viscera One patient was given elorine (tricyclomyl chloride) in a dose sufficient to produce xerostomia but this did not influence peristalic activity of the urinary tract This might lend support to Lapides'[14] suggestions regarding the influence of drugs on ureteral peristalsis One patient with megaloureter was studied and found to have peristaltic activity within the range of normal It is interesting to note that the amplitude of the peristaltic waves was significantly higher in the lower third of the ureter in our series This may indicate one reason why ureteral-vesical reflux does not normally occur However, when the ureter is reimplanted into the bladder at the level of the midureter, not only is the anatomic value at the ureteral-vesical junction sacrificed but the strongest and most active peristaltic segment may be lost as well Two causes for reflux are probably then present, one enhancing the other

SUMMARY

The basal pressure and peristaltic activity in the renal pelvis, mid and lower ureter were studied in 17 normal adult females

Basal pressures, amplitude, frequency, and configuration were noted and

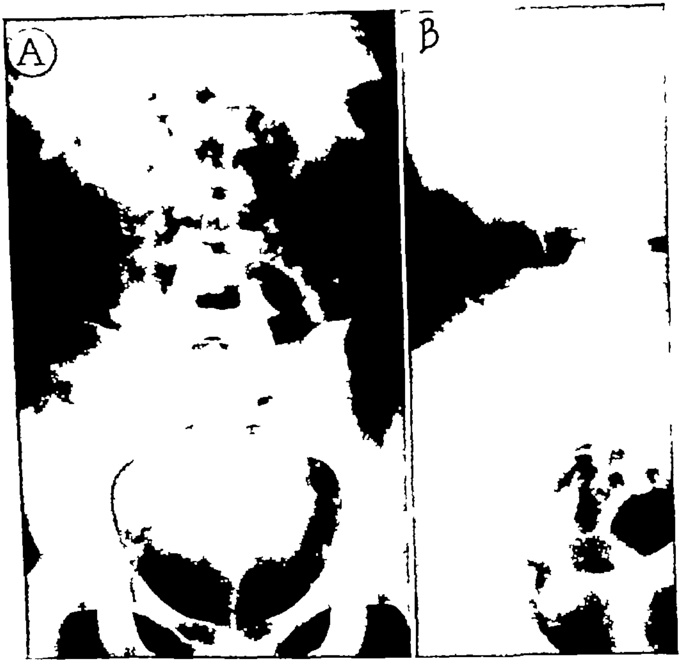

FIG 1 Case 1 Excretory urograms *A*, 5 days after right ureteral ligation *B*, 18 months after deligation

ruptured ectopic pregnancy Bleeding was noted from a right ovarian cyst, and a right oophorectomy was performed Hemostatic sutures were placed lateral to the right uterosacral ligament Postoperatively, there was a large amount of abdominal distention but at no time did the patient's temperature exceed 100F On the second postoperative day the patient complained of pain in the right lower quadrant radiating to the right flank Excretory urograms on the fourth postoperative day showed right hydronephrosis and a normal left urinary tract (fig 1) On the fifth postoperative day, cystoscopy revealed an impassable obstruction 6 cm above the right ureteral orifice The patient was immediately taken to surgery, and the abdomen reopened The area of the right ureter was exposed and two ligatures were removed from around the ureter A No 5 catheter still could not be passed beyond the obstruction, but with a stylet in the lumen of the catheter it was forced up to the right kidney pelvis A profuse flow of urine was obtained The ureteral catheter was then tied to an indwelling Foley catheter placed in the bladder

The patient had a normal postoperative course except for temperature to 100F and slight abdominal distention The ureteral catheter was removed on the eighth postoperative day On the following day, excretory urograms showed normal function and drainage of both kidneys

The patient remained completely asymptomatic, and an excretory urogram taken on September 26, 1956, eighteen months postoperatively, again showed normal function and drainage of both kidneys (fig 1) A No 10 bulb was passed up to the right kidney pelvis with ease Urinalysis was normal the urine is infected In the light of our experience, we would like to add another guidepost, namely, the development of hypertension

The usual picture is that of unilateral complete occlusion, with the development of pain in the kidney area, abdominal distention, fever, and a normal urinary output The diagnosis is made by observing in the excretory urogram decreased function and dilatation of the upper urinary tract on the affected side and the demonstration of an obstruction on ureteral catheterization Although urinary fistula was the first positive sign in 53 per cent of ureteral injuries reported by Patton (1952), no fistula occurred in our series of 5 cases

A high index of suspicion of unilateral ureteral injury is necessary, especially in those cases of pelvic surgery where the patient runs a stormy postoperative course A routine excretory urogram should help detect many unsuspected cases of ureteral injury

CASE REPORTS (TABLE 1)

Case 1 The patient, E L, was a 27-year-old Negro woman On January 7, 1955, an exploratory operation was done with the preoperative diagnosis of

TABLE 1

Case	Original Operation and Diagnosis	Signs and Symptoms	Days Ligated	Results of Deligation
1 E L 27 CF	Right oophorectomy for hemorrhage into small ovarian cyst 1–7–55	1 Pain right kidney—2nd day 2 Low grade fever 3 Moderate abdominal distention 4 No hypertension	5 days	Excellent 19 months
2 J S 27 CF	Total hysterectomy for small fibroid 2–11–55	1 Pain right kidney—2nd day 2 No fever 3 Moderate abdominal distention 4 No hypertension	6 days	Excellent 18 months
3 B W 31 CF	Emergency hysterectomy for placenta accreta 11–29–55	Hypertension only	33 days	Excellent 9 months
4 M H 52 CF	Difficult subtotal hysterectomy and bilateral salpingo oophorectomy for gr 4 P I D 4–12–56	High index of suspicion only	7 days	Excellent 4 months
5 J V D 41 WF	Total hysterectomy & Marshall-Marchetti for fibroids & stress incontinence 8–3–56	1 Left kidney pain—1st day 2 No fever 3 No abdominal distention 4 No hypertension	5 days	Excellent 2 months

with ease The patient has been completely asymptomatic and the urine has remained normal

Case 3 On November 29, 1955, B W , a 29-year-old Negro school teacher, was admitted to the hospital in active labor, with a normal blood pressure of 110/70, and spontaneously delivered a nonviable 24-week-old-fetus After delivery the patient continued to bleed vaginally, and manual examination revealed a placenta accreta She went into shock, and received 2500 cc blood while an emergency hysterectomy was performed She had a normal postoperative course and was discharged on the seventh postoperative day

Two weeks later the patient complained of violent headaches, palpitation, and blurring of vision Physical examination revealed a blood pressure of 210/120, widening of the area of cardiac dullness, and arteriolar spasm with patchy exudate in her eyegrounds Urinalysis showed 2 plus albumin, with numerous leukocytes and casts There was no history of costovertebral pain or symptoms of bladder irritation

She was readmitted to the hospital on December 30, 1955, where an excretory urogram showed a nonfunctioning left kidney (fig 3) On cystoscopy, a catheter met an obstruction 8 cm above the left ureteral orifice On January 1, 1956, 33 days after her initial surgery, the patient's abdomen was opened and the lower left ureter was explored When a catheter was moved up the left ureter through a cystoscope, the ureter was found bound down in a mass of scar tissue and occluded by a chromic catgut suture After the ligature was removed, the lumen of the ureter was still occluded and the ureteral catheter could not be passed The fibrotic area was accordingly incised, and the catheter was slipped up to the left kidney pelvis with ease and then removed A second opening was made 3 cm above the area of the ligature, and a No 12 T-tube was inserted,

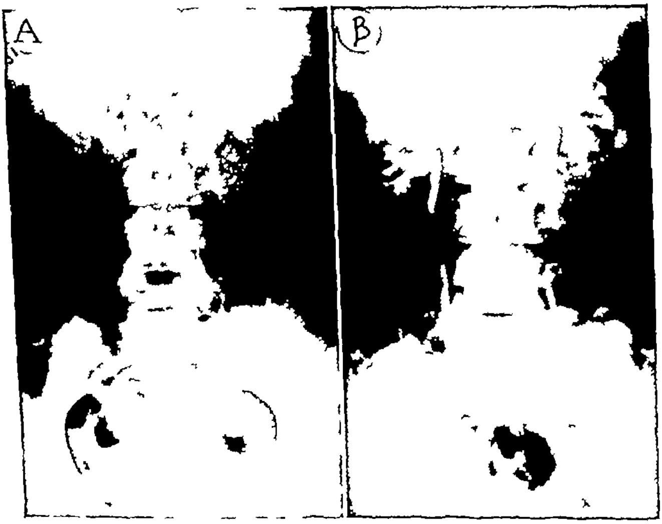

Fig 3 Case 3 Excretory urograms *A*, 32 days after ureteral ligation *B*, 6 months after deligation

Case 2 J S was a 27-year-old white woman On February 11, 1955, a total hysterectomy was performed, without difficulty, for a fibroid uterus Immediately after surgery, the patient became distended, and a Wangensteen suction apparatus was inserted for 36 hours At no time did the temperature rise above 100 4F A normal urinary output was maintained, and the blood pressure was recorded twice at about 100/70 On the second postoperative day, the patient complained of pain in the right kidney area She had no other urinary complaints On the sixth postoperative day, excretory urograms (fig 2) showed right hydronephrosis and a normal left kidney Cystoscopy was performed on the same day and a catheter met an impassable obstruction 10 cm above the right ureteral orifice The patient was immediately taken to surgery and the previous incision was reopened With the aid of a catheter passed up to the right ureter through a cystoscope, the surgeon was able to identify the ureter with a ligature around it After this suture was removed, the catheter entered the kidney pelvis with ease and was tied to an indwelling urethral catheter The patient then had a normal postoperative course The ureteral catheter was removed on the fourteenth postoperative day and excretory urograms on the following day showed normal function and drainage of both kidneys

Subsequent periodic excretory urograms (fig 2) were normal Nineteen months after the deligation, a No 10 bulb could be passed into the right kidney pelvis

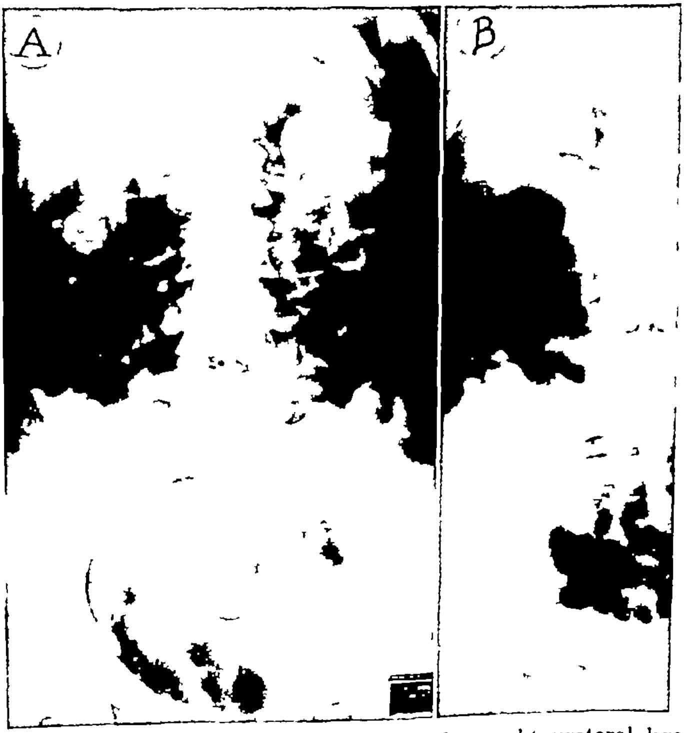

FIG 2 Case 2 Excretory urograms *A*, 6 days after right ureteral ligation *B*, 18 months after deligation

with ease The patient has been completely asymptomatic and the urine has remained normal

Case 3 On November 29 1955 B W a 29-year-old Negro school teacher was admitted to the hospital in active labor with a normal blood pressure of 110 70 and spontaneously delivered a nonviable 24-week-old-fetus After delivery the patient continued to bleed vaginally, and manual examination revealed a placenta accreta She went into shock and received 2500 cc blood while an emergency hysterectomy was performed She had a normal postoperative course and was discharged on the seventh postoperative day

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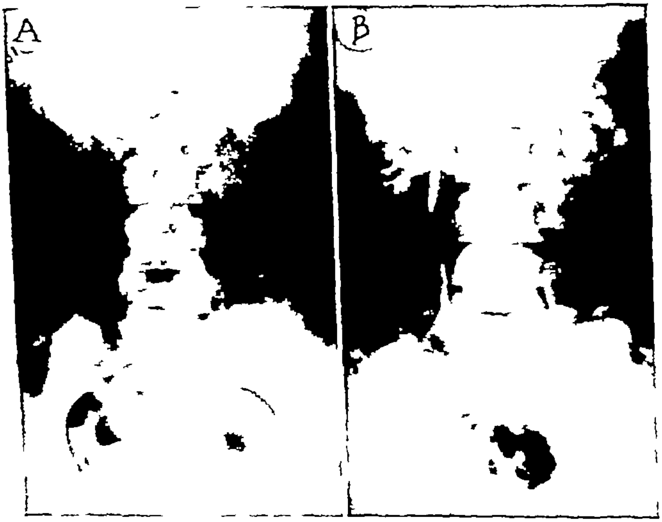

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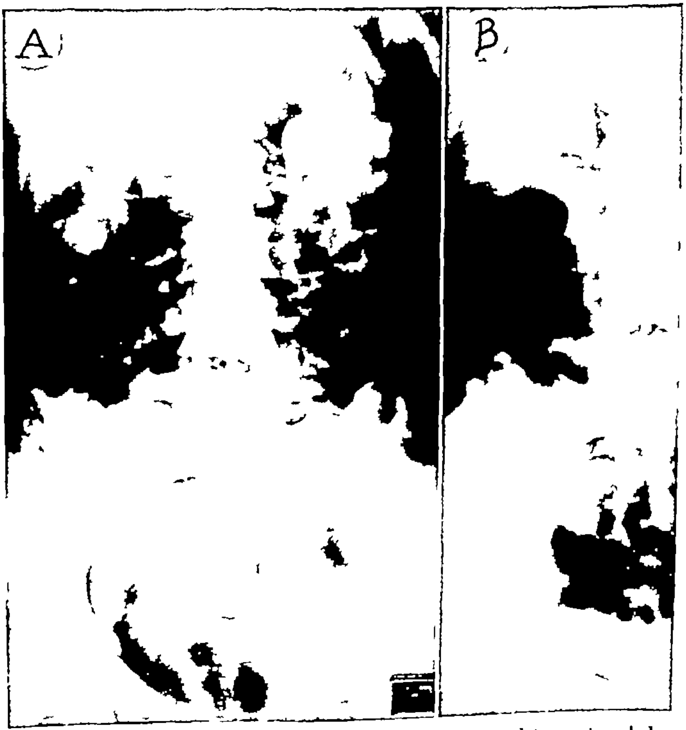

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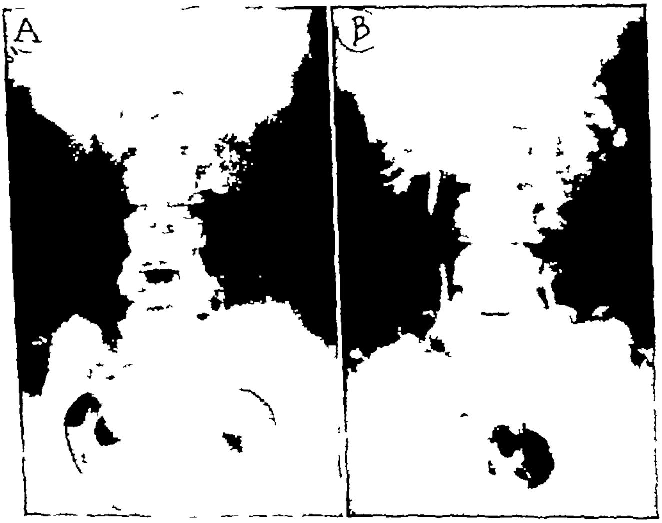

FIG 3 Case 3 Excretory urograms A, 32 days after ureteral ligation B, 6 months after deligation

with one aim going up to the kidney pelvis and the other down toward the bladder The incised portion of the ureter was approximated loosely with 000 chromic catgut suture, and the T-tube was brought out through a stab wound in the left lower quadrant Postoperatively, there was copious diuresis of 3 to 4 liters daily from the T-tube The urine was of low specific gravity, but this gradually increased to normal during the subsequent three weeks The blood pressure declined to 120/80 on the fifth postoperative day, and at no time did it rise above this level The T-tube was inadvertently removed on the eighth postoperative day, and a No 6 ureteral catheter was passed up to the left kidney pelvis through the cystoscope and left indwelling until the thirty-first postoperative day The eyegrounds were normal after the twenty-first postoperative day The patient was discharged on the thirty-fifth postoperative day, completely asymptomatic, with sterile urine

On September 19, 1956, nine months postoperatively, the patient remained completely asymptomatic, and the blood pressure was 120/82 Urinalysis and excretory urograms (fig 3) were entirely normal, and a No 10 bulb slipped easily up the left ureter

Case 4 The patient was M H, a 52-year-old Negro woman On April 12, 1956, a difficult subtotal hysterectomy and bilateral salpingo-oophorectomy were performed for an old pelvic inflammatory disease The cervix of the uterus could not be removed because of the large amount of induration in the area Copious bleeding on the left side of the pelvis was controlled with suture ligature

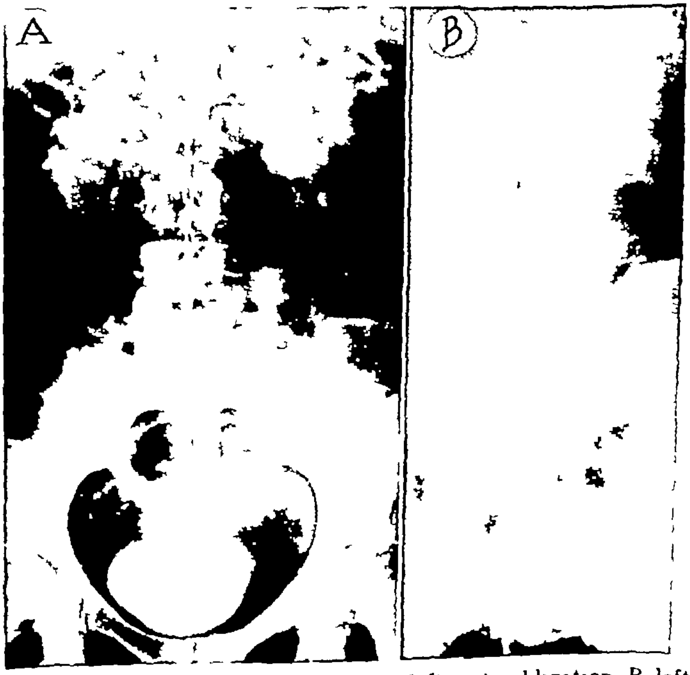

FIG 4 Case 4 *A*, excretory urogram 7 days after left ureteral ligation *B*, left retrograde pyelogram 4 months after deligation

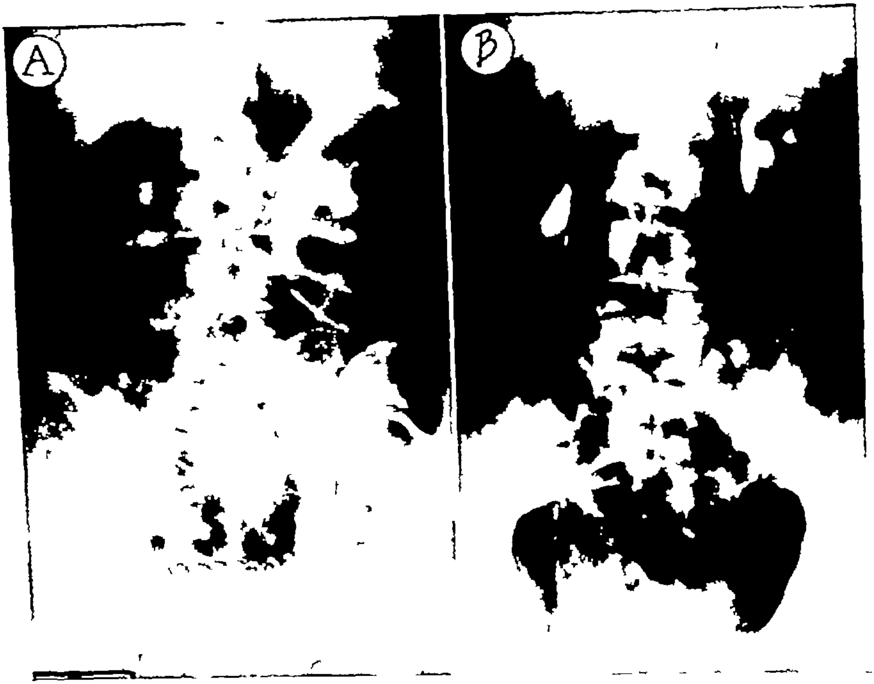

FIG 5 Case 5 A excretory urogram 4 days after left ureteral ligation *B*, retrograde pyelogram 2 months after deligation

Postoperatively, the patient displayed no distention or kidney pain and only low grade fever of 100F Blood pressure, which was 150 70 at the time of admission, remained the same throughout her hospital stay Because of previous past experience and a high index of suspicion before she was discharged from the hospital a routine excretory urogram was performed and showed a left hydronephrosis and hydroureter (fig 4) Cystoscopy on April 19, 1956, the seventh postoperative day, revealed an impassable obstruction of the left ureter 10 cm above the orifice The incision was immediately reopened and with the cystoscopist moving the ureteral catheter at the area of obstruction the surgeon was easily able to find and remove the ligature from around the ureter A No 7 catheter then slipped into the left kidney pelvis and was tied to a Foley catheter The patient was discharged with the ureteral catheter in place on the fifth postoperative day

The ureteral catheter slipped out on the following day and was replaced by a No 8 catheter passed into the left kidney pelvis This was retained for a total of 21 days Four months postoperatively, the patient was completely asymptomatic and a No 10 catheter could be passed easily up the left ureter to the left kidney pelvis Urinalysis was entirely normal Left kidney function and left retrograde pyelogram (fig 4) were also normal

Case 5 On August 3 1956, J Y D, a 41-year-old white housewife, had a total abdominal hysterectomy and Marshall-Marchetti bladder suspension for small fibroids and stress incontinence There was no unusual bleeding, and the operation proceeded smoothly

On the following day, the patient complained of pain in the left kidney area, accompanied by a moderate amount of abdominal distention There was no fever An excretory urogram on the fourth postoperative day showed a normal right urinary tract with delayed function and dilation of the left kidney and ureter down to the area of the left ureterovesical junction (fig 5) Cystoscopy revealed the entire trigone to be raised toward the roof of the bladder, and it was impossible to catheterize the left ureter On August 8, 1956, the fifth postoperative day, the patient was re-explored It was found that a suture from the periosteum of the pubis had encircled the left side of the trigone and the left ureteral orifice This was released, and a cystoscopist was able to pass a catheter up to the left kidney pelvis with ease After an uneventful postoperative course, the splinting ureteral catheter was removed on the fifth postoperative day

On October 9, 1956, two months after deligation, there were no complaints other than some mild discomfort in the left lower quadrant Urinalysis, left kidney function, and left ureteropyelogram were entirely normal (fig 5)

REVIEW OF THE LITERATURE

There is extensive literature on the incidence and treatment of ureteral injuries Herman (1923) advised "wise inactivity" in unilateral ligation which was asymptomatic and nephrectomy if the ligation was symptomatic In bilateral ureteral ligation, however, he favored deligation, since this had a lower mortality rate (25 per cent) at the time than preliminary nephrostomy (50 per cent) The final results of deligation were also better (75 per cent cured), since only 20 per cent were cured after later reimplantation of the ureters into the bladder

Feiner (1938) collected 260 cases of ureteral injuries from the literature during the period from 1925–1936, with 236 unilateral injuries The cause of these 236 injuries, and the secondary operation for treatment are recorded, but in not one single instance was deligation attempted, despite the presence of 18 ligated ureters He reported two personal cases of bilateral deligation, with 100 per cent mortality, and strongly advised nephrostomy, with subsequent ureteral anastomosis or bladder implantation

Newell (1939) reported 14 cases of unilateral ureteral injuries on the gynecology services of Barnes Hospital from 1915 to 1939 There were seven ligated ureters, six were found incidentally at autopsy, and one was treated early by nephrostomy In one case, deligation for bilateral ureteral ligation was performed on the fourth postoperative day, but the patient expired with sepsis nine days later He advised nephrostomy, and ureteral reconstruction at a later date

Herman and associates (1946) encountered 58 papers on ureteral injuries from 1936 to 1946, and reported 15 cases of their own, none of which were treated by deligation

Moore (1948) remarked about the wide divergence of opinion regarding deligation In a review of 23 articles dealing with ureteral injuries, 8 authors definitely advised against deligation, 11 advocated it, and 4 did not mention it Moore states that deligation is an excellent procedure, if the patient is in good condition and if the surgeon and urologist work in close co-operation from above and below He reported a case of bilateral ligation of the ureters which was successfully treated by unilateral nephrostomy on the third postoperative day followed by bilateral deligation three days later

Niceley (1950), in discussing management of late ureteral injuries, mentions that the ureter may be deligated, repaired, or transplanted to the bowel or bladder He presented four cases in which ureteral injuries were suspected by the operating surgeon but, because urological consultation was deferred, nephrectomy instead of deligation resulted

Patton (1952) presented 36 cases of ureteral injuries and, although he mentions that in certain instances deligation is feasible, temporary nephrostomy still remains the safest course None of his cases were treated by deligation

Aschner (1953), after an excellent review of the literature, advises nephrostomy following unilateral ureteral ligation He reported 11 cases which were treated in the usual manner, with good results in the majority

St Martin and colleagues (1953) reported 26 cases of ureteral injury, secondary to gynecological surgery, with deligation in two cases In one case a nephrostomy was performed on the nineteenth day, and on the forty-fourth day transperitoneal ureterolysis and cystoscopic passage of a splinting ureteral catheter were successfully performed They mention that deligation is technically much easier if preliminary diversion of the urinary stream has been performed

Creevy (1953) advises prompt exploration of lower ureteral injuries with deligation or other definitive therapy He recommends preliminary nephrostomy only if the patient's general condition is poor

Conger and associates (1954) treated two cases of bilateral ureteral ligation successfully by immediate deligation and reimplantation of both ureters in the bladder In 11 unilateral injuries reported, no opportunity for deligation was present in these complicated cases

McKay and associates (1954) reported two cases of unilateral injury treated successfully by deligation On the sixth postoperative day the abdomen was reopened and, while an assistant passed a catheter up the ureter to help identify it, the ureter was deligated and splinted for one week In the second case, a ureterovaginal fistula developed on the twelfth postoperative day, and was treated several days later by deligation of the ureter, excision of scarred tissue, and reimplantation of the ureter into the bladder

Landsteiner (1954) reported 2 cases of bilateral ureteral ligation, with one case treated unsuccessfully by deligation and then reoperated on with successful reimplantation of both ureters into the bladder The second case was treated by bilateral nephrostomy with successful plastic repair of the lower ureters at a later date His remaining seven cases of ureteral injuries were complicated by urinary extravasation, necessitating late reimplantation of the ureters into the bladder

Howkins (1954), in a comprehensive discussion of ureteral injuries, does not recommend deligation as an advisable procedure

Falk (1954) also discourages deligation as a difficult and dangerous procedure Since the wound is filled with blood and plastic exudate, he believes that there is great danger of further injuring the ureter because of accompanying poor exposure

Coplan and colleagues (1954) reported 15 ureteral injuries, and emphasized the use of the ureteral transilluminator (diverticulite) in the distal portion of the ureter while the surgeon works in the abdominal incision

Wishard (1955) unsuccessfully attempted bilateral ureteral deligation from above 24 hours after a vaginal hysterectomy Cutaneous ureterostomies were performed, but the patient died in 36 hours He believes preliminary nephrostomies advisable

Rusche (1956) reported a case of successful deligation and removal of acute angulation of the ureter on the third postoperative day

Burns and Peiser (1956) emphasized the necessity of individualizing each case of ureteral injury, taking into account the age and general condition of the patient, functional capacity of both kidneys, curability of the primary surgical lesion, and the economic status of the patient, along with the knowledge of the exact site and type of injury He does not believe in early deligation because local tissue reaction usually makes the procedure difficult and unsatisfactory He recommends early nephrostomy, and later definitive therapy after the tissue reaction in the area of injury has subsided

HOW LONG CAN A KIDNEY SURVIVE AFTER LIGATION?

The period of viability of a kidney after unilateral complete ureteral ligation has not been definitely determined A review of the literature reveals that much work has been done on the production of hydronephrosis, both clinically and experimentally On the other hand, there are few clinical and practically no experimental investigations on the results of restitution of the kidney after temporary hydronephrosis

Clinical investigations of the recovery of the kidney after temporary hydronephrosis have been difficult to evaluate because insufficient information is available concerning the duration and cause of hydronephrosis, the time interval between ligation and deligation, and whether infection or fistula formation ensued

While several articles have been written about the effect of ureteral ligation on the development of hypertension and early recovery of renal function, very little has been written about the resulting hydronephrosis and surviving kidney

Hinman's monumental work (1934) on hydronephrosis is our only major source of information concerning restitution of the kidney after experimental hydronephrosis Working with dogs, cats, and rats, Hinman ligated the ureter near the bladder and, at various intervals up to 90 days, reimplanted the ligated ureter into the bladder He found that the experimental animal did not survive a complete ureteral obstruction of longer than 2 to 3 weeks, if the opposite kidney was removed at the time of implantation Hydronephrosis of 3 or 4 weeks' duration may repair sufficiently to carry on total function, with survival of the animal, if the opposite normal kidney is not injured for several months after the reimplantation The animal may survive hydronephrosis of 30 to 90 days' duration, if the burden of excretion is gradually shifted to it by slow destruction of the opposite normal kidney Thus, the theory of renal counterbalance was originated Hinman also showed that the repair of hydronephrosis is manifested microscopically by the return of less injured groups of glomeruli and tubules to a more normal appearance, with some hypertrophic changes The functional recovery of the kidney was proportional to these microscopic changes

Fylling (1951) has shown that rats' kidneys could survive after 30 days of occlusion Kerr (1956) obstructed the ureters of dogs for four weeks, and noted maximum recovery of the kidney in thirty days, as determined by glomerular filtration and effective renal plasma flow However, the ability of the kidney to concentrate urine was still impaired after 30 days

Our third case was ligated for 33 days and recovered normal function on excretory urograms Since it is well known that hydronephrosis develops more rapidly in smaller than in larger animals, what is the rate of development and recovery of the human kidney? The answer still is unknown

DISCUSSION

It is highly advisable for surgeons to order routine excretory urograms in all patients who have had difficult pelvic surgery or in whom ligation of the ureter is suspected Palpation of the kidney area should become as routine as examination of the abdominal wound Certainly, many relatively asymptomatic ureteral injuries would be detected early

If in any of our five patients a ureteroabdominal or ureterovaginal fistula had developed, would our treatment have been different? If the patient has a large abdominal mass and appears septic and in poor general condition, preliminary nephrostomy still remains the treatment of choice, with incision and drainage of the urinary abscess, if necessary However, if the patient is in good general condition, deligation and splinting of the ureter would still be our procedure of choice Certainly, one could obtain satisfactory urinary drainage with return of kidney function through a splinting ureteral catheter as well as through a nephrostomy tube In addition, the patient has been saved the expense and risk of multiple operations Also, reimplantation of the lower ureter by the best of surgeons is successful in only 90 per cent of the cases

Our third case had no signs or symptoms, except those attributable to hypertension In our review of the literature, we have been unable to find any such similar case Grollman and associates (1949), working with dogs, showed that unilateral ligation of the ureter causes a temporary rise in blood pressure, probably due to renal congestion and the release of a pressor substance into the bloodstream He is of the opinion that, had this patient survived the malignant hypertension, which was unlikely, her blood pressure probably would have returned to normal in several months, after the kidney had been destroyed and

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Deligation as it has been practiced in the past by the average surgeon, without the help of a urologist, is undoubtedly dangerous The patient is usually in very poor condition, and much time is lost in attempting to find the ligated ureter in a maze of serous exudate and friable tissue However, if the urologist moves the obstructed ureter with a catheter from below, the offending ligature can easily be found, and removed, and the ureteral catheter passed up to the kidney pelvis and left indwelling as a splint With this type of teamwork, the operation is extremely simple and certainly very gratifying

SUMMARY

We have treated 5 cases of unilateral surgically ligated ureters by deligation as soon as the diagnosis was made The results have been excellent

With close co-operation between the abdominal surgeon working above and the urologist working below, deligation is a simple and innocuous procedure

Postoperative hypertension in a patient following pelvic surgery may be an early sign of ureteral obstruction

We wish to thank Mrs Elinor Reinmiller, librarian of Southwestern Medical School of the University of Texas, for her kind co-operation in preparing the bibliography We are also grateful to Drs H A O'Brien, J D Mitchell, Jr and J L Denman for permitting us to report the fifth case of this series

ADDENDUM

Two more cases of ligated ureters have been treated by deligation and ureteral splinting Again the results have been excellent, with no evidence of ureteral structure or kidney damage

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URETERAL REPAIR AND THE SPLINT

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Urologic surgeons avoid splinting the ureter whenever possible, fearing the secondary effects of an in-lying tube An infection caused by "hospital organisms," resistant to most antibiotics, is perhaps the most common result of intubation, and the most difficult to correct Tubes are not only uncomfortable for the patient but psychologically upsetting to him as well A foreign body reaction occurs around the tube and calculi may form Finally, the ureteral musculature hypertrophies after five or six weeks[1] of ureteral splinting and the functional characteristics of the ureter are altered In spite of these disadvantages, splints do serve some useful purposes Knowledge and evaluation of the advantages, disadvantages and technical application of the ureteral splint are important to the surgeon, that he may know *how* to use a splint, and *when*

The student of ureteral repair is dependent in large part upon animal experimentation, deductions drawn from recorded clinical experience are less reliable Each patient with ureteral disease must be evaluated separately, since the condition varies in each case, as does the choice of surgical technique Choice of technique is subject to the enthusiasms of proponents of a particular form of surgical management, and to the current fashions in the field of urology Hence, even though the results of animal experimentation are not necessarily directly applicable to operations in human beings, such experimentation is needed for an understanding of the basic processes in ureteral healing

THE CLINICAL PROBLEM (FIG 1)

We can visualize the healing of a ureteral defect by comparing it with the healing processes following a third degree burn of the skin If new epithelium can grow quickly over the defect from the skin edges, overgrowth of granulation tissue is avoided and the amount of final scarring decreased If epithelialization is inhibited, by irritative dressings for example, granulation tissue is heaped up and extensive fibrosis and contracture are inevitable Our experimental work on the ureter shows a similar parallel between the ease with which primary epithelialization can take place and the completeness of the final reconstitution of the muscular coat, which, we have shown, occurs by actual smooth muscle regeneration [2, 3]

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Read in part before the Annual Congress, Los Angeles Urologic Research Convention, November 15, 1956

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[2] Oppenheimer, R and Hinman, F , Jr Ureteral regeneration *Contracture vs hyperplasia of smooth muscle* J Urol 74 476–484, 1955

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THE PROBLEM

TO OBTAIN
AN *EPITHELIAL TUBE QUICKLY*

↓

TO ALLOW
MUSCULAR REGENERATION

↓

TO AVOID
FIBROSIS AND STRICTURE

FIG 1

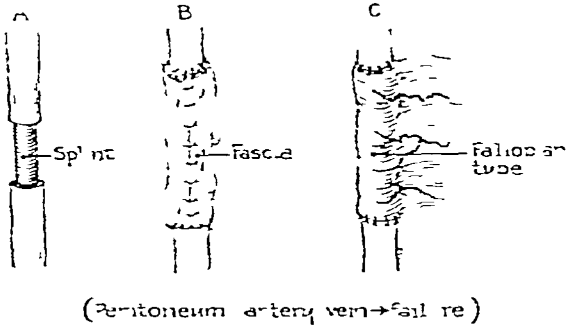

FIG 2 Epithelialization occurs 1) across short splinted gap and 2) inside fascial graft but 3) does not replace established epithelium of another type as in the ileum or fallopian tube

PRIMARY EPITHELIALIZATION

New epithelium may cover the ureteral defect by one of several routes (fig 2) Before 1926 Peck[4] and McArthur[5] in clinical cases and Joannides and Holmes[6] in experimental animals showed that an appreciable defect in the ureter (about ¾ inch) would heal over a splint (fig 2 *A*) by epithelial growth from the cut ends We have made similar clinical observations[7]

If a fascial graft is interposed in the gap[8] (fig 2 *B*) its interior becomes epithelialized by new growth from the severed ends of normal ureter The same is true if the tube is lined with peritoneal mesothelium[9] However if the graft is

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[4] Peck C H Treatment of obstructions of the upper ureter and early hydronephrosis Ann Surg 83 260–266 1926

[5] McArthur L L A new and simple repair of ruptured or strictured ureters Surg, Gynec & Obst 41 719–721 1925

[6] Joannides M and Holmes C K Uretero-ureteral anastomosis an experimental study Journal Lancet 45 470–473 1925

[7] Howard F S and Hinman F Jr The ureteral splint in the repair of ureteropelvic avulsion J Urol 68 148–157 1952

[8] Lord J W Stefko P L and Stevens A R On bridging a gap in the ureter by means of a free fascial transplant over a straight vitallium tube an experimental study J Urol 49 249–257 1943

[9] Strauss A A An artificial ureter made from the abdominal wall a preliminary report of an experimental study Surg, Gynec & Obst 18 78–84 1914

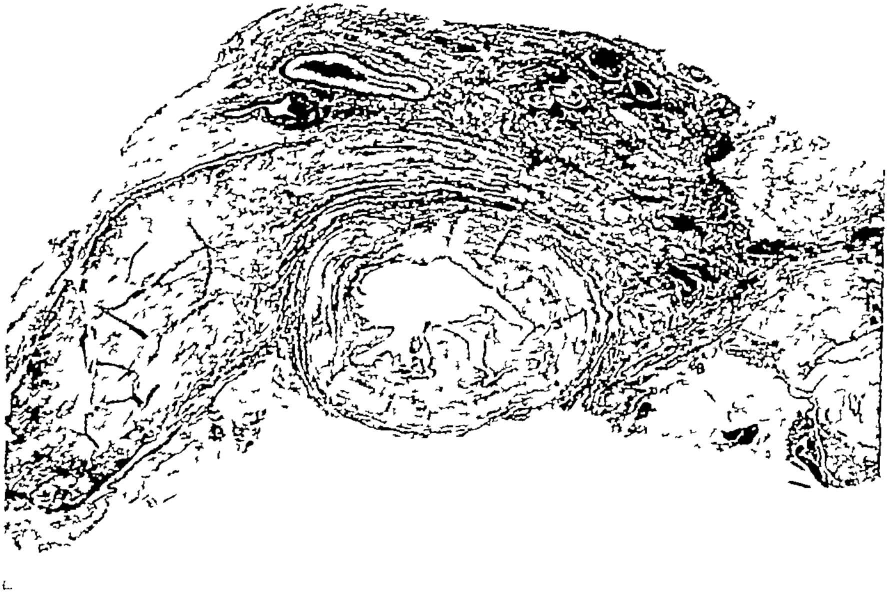

FIG 3 Cross section of dog ureter (No 116A) 6 weeks after simple longitudinal slit (ureterotomy) Note complete epithelialization and normal muscle coats

composed of tissue already lined with epithelium (fig 2, *C*), no new ingrowth occurs This has been shown to be true in the ileum and the fallopian tube[10]

If a strip of ureter bridges the defect, new epithelium will spread rapidly over an in-lying splint[11] If a splint is not provided, epithelium will restore the ureteral lumen more or less adequately, depending upon the size of the defect and upon other factors later to be discussed in detail

For example, a simple slit (as for ureterolithotomy) heals at once with little evidence of reaction (fig 3) A larger defect, as studied by Kaïris and Perlmann[12] in 1927 (fig 4) heals in a similar normal fashion A very large defect, such as Hamm and Weinberg[13] created in dogs, heals less satisfactorily Figure 5 shows such a lesion after healing Note the abnormal wall with partial absence of muscular elements and deposition of cartilage

What do these procedures have in common? They all provide a scaffold for the regrowth of the epithelium It may be a splint, a graft, a tube, or a bed of retroperitoneal fat—but something is provided upon which the epithelium can grow to reform a tube rather than spreading as a sheet out over the retroperitoneal connective tissue

[10] Sanders, A R and Schein, C J The epithelial morphology of autogenous grafts when utilized as ureteral and vesical substitutes in the experimental animal A collective review J Urol 75 659–664, 1956

[11] Davis, D M Intubated ureterotomy, a new operation for ureteral and ureteropelvic stricture Surg, Gynec & Obst, 76 513–523, 1943

[12] Kaïris, Z and Perlmann S Klinische und experimentelle Studien über die Heilung der Nierenbecken und harnleiterwunden Ztschr f Urol, 21 659–669 1927

[13] Hamm F C and Weinberg S R Experimental studies of regeneration of the ureter without intubation J Urol, 75 43–51, 1956

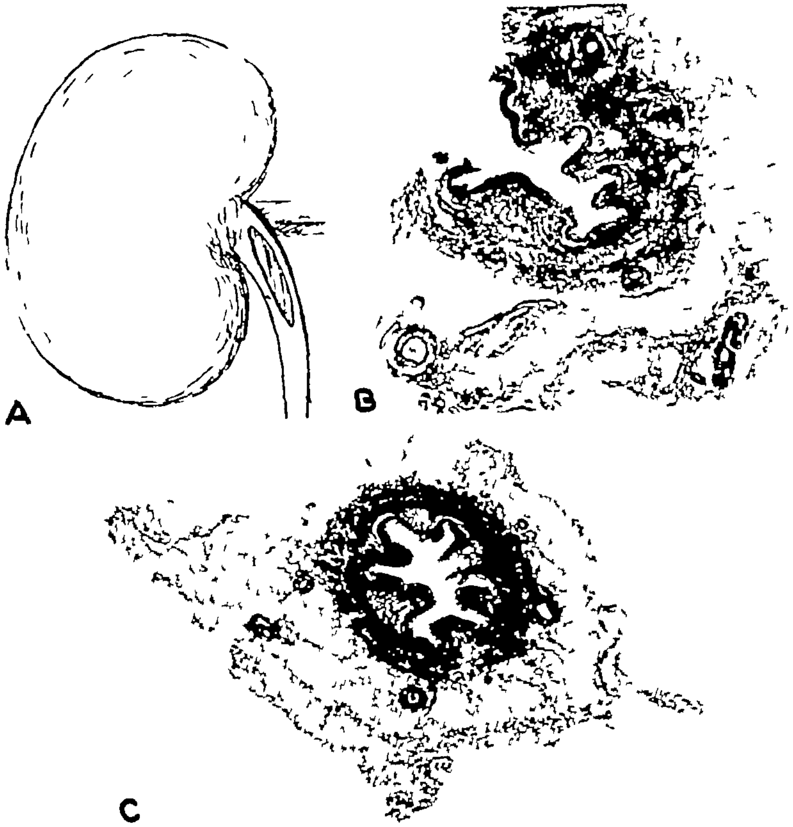

Fig 4 *A*, diagram of portion of ureter resected *B*, cross section, showing surgical defect *C*, cross section 2 months later, showing essentially normal reconstitution of ureter (From Kaïris and Perlmann [12])

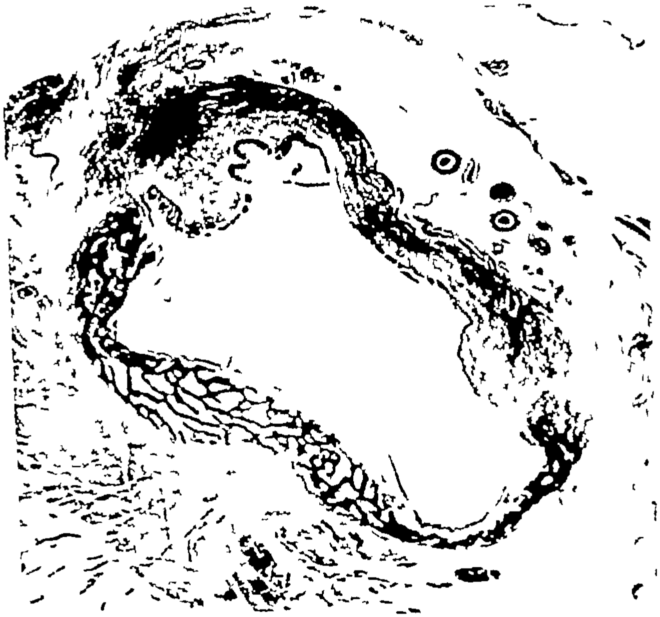

Fig 5 Cross section of ureter 5 weeks after subtotal excision, without splint Note ab- (From Hamm and Weinberg [13])

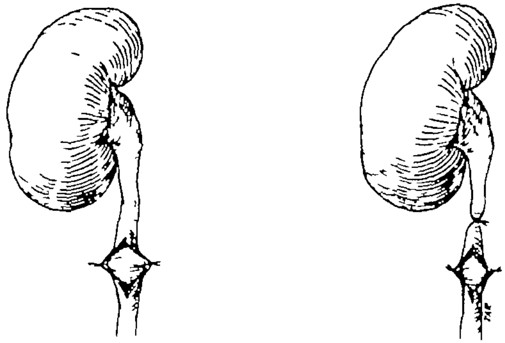

FIG 6 *A*, ureter fixed open, unligated *B*, same, proximally ligated[14]

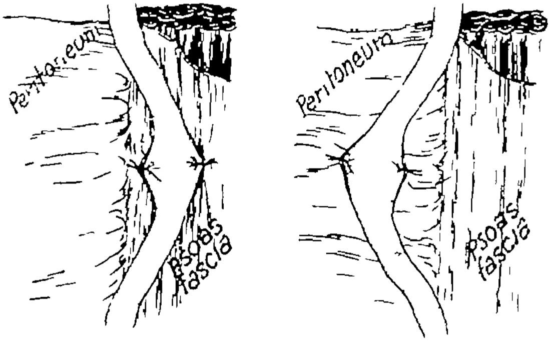

FIG 7 *A*, ureter fixed open against peritoneum *B*, ureter open against fascia[16]

FACTORS INFLUENCING EPITHELIALIZATION

If we knew the reasons for delay in primary epithelialization, we would avoid some of the poor results in clinical cases Certain factors are important

1 *Urinary leakage* Experiments were designed[14] to exaggerate the ureteral defect and so compare healing with and without urinary flow In dogs, the upper ureter was tacked open against the retroperitoneal surface (fig 6) If the ureter was tied off proximally, healing progressed over a period of 6 to 8 weeks At first, growth of epithelium was slow because of the broad area to be bridged, but it eventually formed a tube, and regeneration of the wall followed If the ureter was not ligated, so that urinary flow continued, healing followed a similar sequence of events, but epithelialization was slower and muscular regeneration less regular than when urine was absent We concluded that the damage from urinary flow was greater than any beneficial hydraulic effects, such as Johanson described for urethral healing[15]

2 *Rigidity of bed* Fat was proposed many years ago as a proper cover for a healing ureteral defect[6] [16] to prevent scarring, fixation with angulation[17] and other complications

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[14] Oppenheimer, R and Hinman, F , Jr The effect of urinary flow upon ureteral regeneration in the absence of splint Surg , Gynec & Obst , **103** 416–422, 1956

[15] Johanson, B Reconstruction of the male urethra in strictures Application of the buried intact epithelium technic Acta Chir Scandinav , Supple 176 1–103, 1953

[16] McIver, R B Plastic surgery of the renal pelvis J Urol , **42** 1069–1083, 1939

[17] Lapides, J and Caffery, L L Observations on healing of ureteral muscle relationship to intubated ureterotomy J Urol , **73** 47–52, 1955

We conducted experiments[1] to visualize the assumed adverse factors Comparison was made between the degree of healing of the dog ureter fixed open against the retroperitoneal surface and that placed in apposition to the fascia (fig 7) Healing against peritoneum went ahead more readily with more nearly normal primary epithelialization than that against fascia Fascial apposition resulted in incomplete epithelialization with consequent incomplete muscle regeneration

These experiments tend to show that a rigid fibrous bed is hostile to the reformation of an epithelial lined tube and hence to adequate regeneration of the ureteral wall

APPLICATION OF EXPERIMENTAL DATA TO CLINICAL PROBLEMS

If the surgeon will conjure up in his mind a picture of the steps in the healing process needed for proper repair and base his reasoning on the results of animal experimentation he can decide at the operating table if a splint is essential advisable or unnecessary

Good primary epithelialization after operations on the ureter or renal pelvis can be secured in one of four ways 1) by reapproximating the edges with sutures 2) by allowing juxtaposed edges to fall together 3) by splinting or under certain circumstances 4) by omission of the splint

1 *Repair by reapproximation of edges with suture* An example would be a ureteropyeloplasty such as the Foley-Y or Culp-Scardino operations Splints are not necessary if the repair is reasonably water-tight if necrosis of the edges has been avoided and if the suture line does not obstruct the lumen

2 *Repair by merely allowing the cut edges to fall back together* A ureterolithotomy is a typical instance If only slight leakage and pooling are anticipated and if the ureter is normal and of adequate caliber splinting is not desirable

3 *Repair over splint* Davis has fostered intubation for extensive narrowings at and below the ureteropelvic junction as an alternative to plastic procedures (such as pyeloplasty) or non-intubation

The experimental data indicate that a splinting tube had best be used if the ureteral wall is diseased or abnormally narrow if it must lie in a fibrous bed or if infection and leakage are prominent

4 *Repair without intubation* Kains[2] and Hamm[2] have shown that repair can occur without splinting and our own experiments[4, 5] indicate that this is possible under very adverse conditions The ureteral wall after such repair however may be abnormal and thus subject to later stenosis Practically it would appear that if the ureteral wall is reasonably normal if the ureter can lie in a fatty bed and if urinary diversion is sufficient to prevent urine from being forced into the healing area then a splint can be omitted

TECHNICAL DETAILS (FIG 8)

Material for splints has been subjected to several experimental studies with conflicting results It is probable that a red rubber urethral catheter is as satisfactory as any other

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[1] Hinman F Jr and Oppenheimer P Ureteral regeneration IV Fascial covering compared with fatty connective tissue J Urol 76 723-735 1956

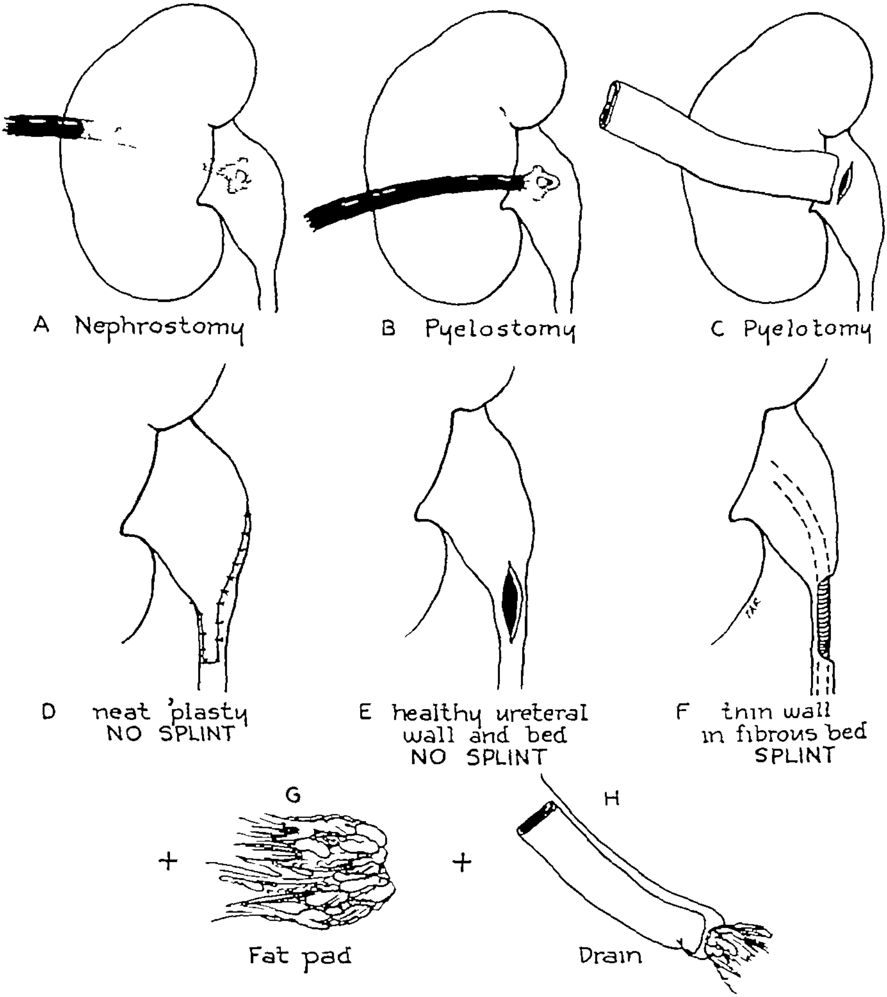

Fig 8 Technical details for ureteroplasty

The size of the splint should be such that it fits the ureter easily Too large a splint damages the wall by ischemic necrosis [19]

The duration of splinting will depend upon the condition of the ureter One week is the minimal period, since this amount of time is needed for epithelialization under the best conditions Six weeks' time is necessary for complete regeneration of all layers of the ureteral wall and is the proper interval if the defect is very large or healing complicated

The distal end may be safely left within the ureteral lumen if the splint is withdrawn one or two centimeters a week This prevents stricture in the lower ureter A nephropexy is done to fix the lower pole of the kidney away from the area of repair

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[19] Weaver, R G The effect of large caliber splints on ureteral healing Surg , Gynec & Obst , 103 590–593 1956

By exposing the ureter and pelvis through a sagittal opening in Gerota's fascia, so that half the perirenal fat lies posteriorly to the plane of approach, the surgeon can provide a fatty bed for the repair (fig 8, *G*) The usual approach along the psoas muscle moves all the fat anteriorly, making enclosure of the ureter within it difficult

Diversion of the urine is important, as we have seen from the experimental data If the repair is water-tight and technically perfect, a simple stab incision in the pelvis with an adjacent Penrose drain may be sufficient (fig 8, *C*) However, if the defect requires time to seal itself (if it is large or if intubation is required), at least a pyelostomy (fig 8, *B*) is necessary, and a nephrostomy (fig 8, *A*) often advisable In addition, regular irrigation (with solution G if necessary for encrustation), a low calcium diet, and perhaps simple suppressive chemotherapy, are useful

Adequate drainage from the site of the defect is of the greatest importance In the course of our experimental work [20] we devised a means of suturing the end of the Penrose drain exactly at the proper site so that it could be removed at any time (fig 8, *H*) This is done by stitching one end of the suture to the drain, then passing the suture through the periureteral tissue and so out alongside the drain The tip of the drain is thus fixed in place, yet it may be removed at any time by release of the long end of the suture If proper placement of the drain is not made, pooling takes place, which, as we have shown experimentally, interferes with healing

SUMMARY AND CONCLUSIONS

The essential processes of ureteral repair have been at least partly uncovered in experimental studies, and form the basis for the use or omission of splinting tubes

A technically perfect repair does not require a splint

If there is doubt as to the viability or orientation of the ureteral edges, a splint is advisable It may be left a short time if only epithelialization is necessary, but can remain as long as 6 weeks if healing must occur by fibrosis and replacement by smooth muscle

The surgeon, by visualizing the reparative processes through which the heeling ureter must pass, can decide for himself those instances in which splinting the ureter will be advantageous

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[20] Hinman F, Jr Accurate placement of the Penrose drain Surg, Gynec & Obst, 102 497, 1956

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CONGENITAL BLADDER NECK OBSTRUCTION IN CHILDREN

ROGERS DEAKIN

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There can be no more rewarding experience than the rehabilitation of a deformed child, the problem of the child with an obstruction of the bladder neck and the attendant deformities and deficiencies of the upper urinary tract should be a challenge to the medical profession It is another frontier, perhaps one of the few remaining, which needs more exploration The fact that this particular deformity is hidden from view should not bar its inclusion in the list of "medical musts" which surround us

It may be that the problems which these children present are too variable and too complex to permit any standardization of procedure, but I believe there is at least a principle involved which requires clarification in our thinking If there is impairment of renal function due to mechanical stress or strain, emphasis should be placed first on protection of the vital area, namely, the kidneys themselves, rather than the bladder, notwithstanding the fact that the bladder is or may have been at fault originally

Through the years I have had a growing conviction that the management of these children was more of a day-to-day improvisation than a careful continuity of effort with adequate long range planning This impression is based on the small group of children for whose care I was responsible, as well as my observation of other children whom I had the opportunity to watch in the St Louis Children's Hospital This feeling of inadequacy and confusion is not wholly personal, however, in that there has been little in the medical literature year after year to indicate that there was a clearer conception anywhere else of what needs to be done for these children

Perhaps, in the satisfaction derived from having improved instruments and radiologic techniques with which to make more accurate diagnoses, we have lost sight of the fact that it is the damage to the kidneys which kills the child, not the bladder neck obstruction A child could live indefinitely with a congenital obstruction of his bladder neck alone, but every minute is precious when dilated kidney pelves and infected kidney parenchyma are destroying renal tissue Delay in intervening to halt the process which is thinning the child's renal cortex is tragic His life span can be measured by the amount of viable kidney tissue left him when our efforts have been concluded

I have stated my belief elsewhere in 1948* that the column of urine in a dilated, elongated ureter was an obstructive factor contributing to destruction of renal parenchyma and a condition worthy of the utmost consideration in the prevention of further damage to an already damaged kidney cortex

Severe degrees of elongation and tortuosity of the ureters may result in a curvature of the lower ureter not unlike the conventional U-trap, further ac-

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Read at annual meeting of South Central Section of American Urological Association, Mexico City, October 28–November 1, 1956

* J Pediat , 33 357–369, 1948

centuating the obstruction in the upper urinary tract Long continued stretch of ureteral musculature must inevitably lessen the ability of the ureteral wall to return to its normal size and mobility The anesthesia in any hollow viscus induced by gradual distention and pressure of ureterectasis also is an undesirable complication to be avoided if possible

The immediate problem, as I see it, is to recognize the urgency of adequate renal drainage and to employ the best surgical means to insure prompt relief of obstruction at the renal level This is a conclusion which, if we accept the "law of rationality" in logic and argument, I should justify by adequate inductive evidence But I do not think I am evading this rule if I state that the importance of the kidneys to life is a fact that requires no substantiation

My difficulty in advancing an argument which would favor upper urinary tract drainage before or instead of lower urinary tract drainage, or which would favor T-tube ureterostomy over nephrostomy in the early surgical management of bladder neck obstruction in children, lies in the fact that there are so few cases on which to base a conclusion I am forced again to take refuge in a reference to a representative standard college textbook on Logic* in which it is stated that science is not concerned exclusively with *inductive* logic The latter seeks to establish truth from the facts of experience—so that a conclusion is drawn from the data obtained in a large series of cases On the other hand, the same text says that *deduction* may be the instrument which we can utilize to predict the future, without requiring a large series on which to base a conclusion It is the encouragement which this statement affords me that leads me to hope I can stimulate you to review critically your own experiences in the management of a child with congenital bladder neck obstruction, and perhaps persuade you to be receptive to the approach to this problem that I present herewith

I do not propose to attempt an exhaustive review of what has been published already on our basic knowledge of congenital bladder neck obstruction The anatomical variations of the bladder neck which produce obstruction have been described very well in all modern urologic texts The deformities of the bladder which are associated with and presumably caused by the obstruction are well known The dilatation, elongation, tortuosity and redundancy of the ureters seen in advanced cases are familiar sights to all of us, as is the hydronephrosis which is present in the kidneys The anatomical pattern varies only in degree in most cases

Nor is the clinical picture likely to be too variable Infection is dominant, malnutrition is inevitable, acidosis frequent and the bladder dysfunction and renal insufficiency are variable, again only in degree

I am also not concerned in this discussion with the various chemical and laboratory procedures in present day use to measure renal function Our knowledge of electrolytes and the role of electrolyte imbalance may not be as complete as it should be, but it is at least sufficient for us to understand much of the physiology of renal dysfunction and to permit an intelligent comprehension of this phase of the problem

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* Lionel Ruby Logic—An Introduction Philadelphia J B Lippincott Co , 1950

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Minor questions may arise, of course, in some areas For instance, there may be disagreement as to why some of these ureters regurgitate while others do not, apparently independent of the amount of upper urinary tract dilatation Or we may disagree as to what we see or think we see cystoscopically or surgically in these tiny bladder necks Opinions about the use of the different antibacterial agents in use are as varied and changing as the restless sea in a brisk "nor' easter "

I have no exact knowledge of the number of children so afflicted It is conceivable that a physician might go through a lifetime of practice without ever encountering such a child In large urban areas supporting hospitals for children, the number of such cases is considerable if our own medical center is any criterion, although these children represent the screening from a large geographic area

There are 56 cases of congenital bladder neck obstruction on file in the record room of the St Louis Children's Hospital covering the period between 1933 and 1955

This does not include any case of urinary retention with or without upper urinary tract damage in which there was neurogenic dysfunction of the bladder associated with accidental trauma, spinal cord tumor, myelomeningocele, epispadias, exstrophy of the bladder, unilateral megalocolon or spina bifida occulta The importance of preserving renal function in these cases cannot be overemphasized, however, and I think that which may be said in favor of upper urinary tract drainage applies as much to this group in most instances as it does to those children in whom a purely mechanical obstruction is at fault

The symptoms and signs in 24 of these 56 children were limited to the bladder neck and bladder, showing no significant upper urinary tract deformities This group ranged from 4 months in age on admission to the hospital to 13 years, with 16 of them 6 years old or more when first seen Fifteen were boys and 9 were girls All but 5 of them were private cases of different staff members All responded to simple transurethral manipulations, usually fulguration or resection, and are not included further in this discussion because they do not fall into the category with marked upper urinary tract dilatation about which we are talking

The 3 girls remaining in the series SSA—D 793, age 6 months, KK—N 1700, age 3 years, and DLS—Z 1761, age 17 months, were all private cases Each showed some reflux initially Each received one or more resections or fulgurations of the bladder neck but none required either cystostomy or upper urinary tract drainage during their respective 3, 4 and 7- year periods of observation Deformity of the kidney pelves compatible with chronic pyelonephritis has been the chief radiologic observation in all of them and intermittent or persistent urinary tract infection the main clinical problem

Pyeloureterectasis, however, has not been a complication in any of them The question may be raised, therefore, if girls with bladder neck obstruction of nonneurogenic origin are subject to the obstructive uropathies of the upper urinary tract which are noted in the male sex

The 29 remaining boys may be divided further into 10 who were private cases, for whom a single staff member was responsible, and 19 ward or charity cases for whom various members of the staff assumed responsibility at different times Eighteen of the 29 were in the 0–3 year age group (62 per cent) when admitted to our hospital, 6 in the 3–7 year age group (21 per cent) and 5 in the 7–12 year age group (17 per cent)

All had severe dilatation of the upper urinary tract As many as 5 staff members shared responsibility in the care of some of these ward cases It may be that the seeming lack of continuity or planning in their management was more apparent than real because of this diversity of responsibility Certainly, in going over the files, there can be no doubt of the sincerity of the consultants as they contended with the various complications that arose during their supervision of these children Moreover, the progress notes in these files provide a dramatic picture of the almost daily problems which beset the pediatrician, urologist and house staff as they struggled with infection, obstruction, azotemia, acidosis and malnutrition in the day-to-day care of these children

I believe that the urinary bladder of some of these patients need never be opened if adequate drainage at the upper urinary tract level has been established, and that there are some advantages in this course of action An exception, of course, would be the child with a large diverticulum of the bladder which required ultimate surgical excision Another exception would be the very young infant whose genitals were too small to admit any form of endoscopic instrument,

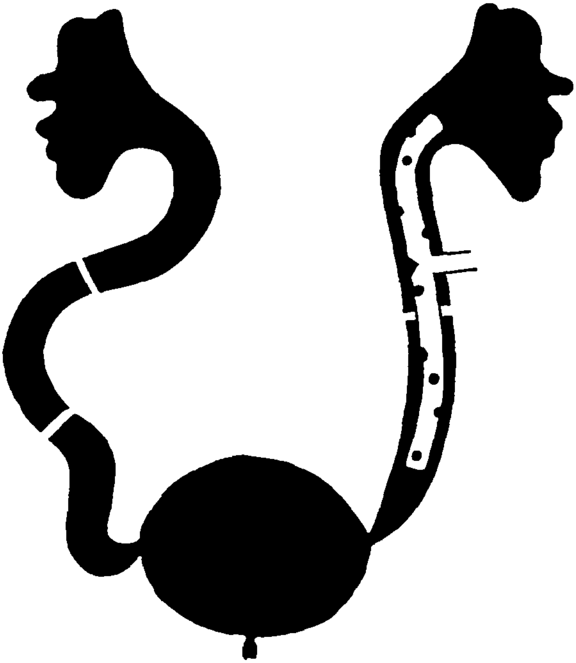

Fig 1 Schematic representation of resection of portion of redundant ureter and T-tube ureterostomy

Minor questions may arise, of course, in some areas For instance, there may be disagreement as to why some of these ureters regurgitate while others do not, apparently independent of the amount of upper urinary tract dilatation Or we may disagree as to what we see or think we see cystoscopically or surgically in these tiny bladder necks Opinions about the use of the different antibacterial agents in use are as varied and changing as the restless sea in a brisk "nor' easter"

I have no exact knowledge of the number of children so afflicted It is conceivable that a physician might go through a lifetime of practice without ever encountering such a child In large urban areas supporting hospitals for children, the number of such cases is considerable if our own medical center is any criterion, although these children represent the screening from a large geographic area

There are 56 cases of congenital bladder neck obstruction on file in the record room of the St Louis Children's Hospital covering the period between 1933 and 1955

This does not include any case of urinary retention with or without upper urinary tract damage in which there was neurogenic dysfunction of the bladder associated with accidental trauma, spinal cord tumor, myelomeningocele, epispadias, exstrophy of the bladder, unilateral megalocolon or spina bifida occulta The importance of preserving renal function in these cases cannot be overemphasized, however, and I think that which may be said in favor of upper urinary tract drainage applies as much to this group in most instances as it does to those children in whom a purely mechanical obstruction is at fault

The symptoms and signs in 24 of these 56 children were limited to the bladder neck and bladder, showing no significant upper urinary tract deformities This group ranged from 4 months in age on admission to the hospital to 13 years, with 16 of them 6 years old or more when first seen Fifteen were boys and 9 were girls All but 5 of them were private cases of different staff members All responded to simple transurethral manipulations, usually fulguration or resection, and are not included further in this discussion because they do not fall into the category with marked upper urinary tract dilatation about which we are talking

The 3 girls remaining in the series SSA—D 793, age 6 months, KK—N 1700, age 3 years, and DLS—Z 1761, age 17 months, were all private cases Each showed some reflux initially Each received one or more resections or fulgurations of the bladder neck but none required either cystostomy or upper urinary tract drainage during their respective 3, 4 and 7- year periods of observation Deformity of the kidney pelves compatible with chronic pyelonephritis has been the chief radiologic observation in all of them and intermittent or persistent urinary tract infection the main clinical problem

Pyeloureterectasis, however, has not been a complication in any of them The question may be raised, therefore, if girls with bladder neck obstruction of nonneurogenic origin are subject to the obstructive uropathies of the upper urinary tract which are noted in the male sex

The 29 remaining boys may be divided further into 10 who were private cases, for whom a single staff member was responsible, and 19 ward or charity cases for whom various members of the staff assumed responsibility at different times Eighteen of the 29 were in the 0–3 year age group (62 per cent) when admitted to our hospital, 6 in the 3–7 year age group (21 per cent) and 5 in the 7–12 year age group (17 per cent)

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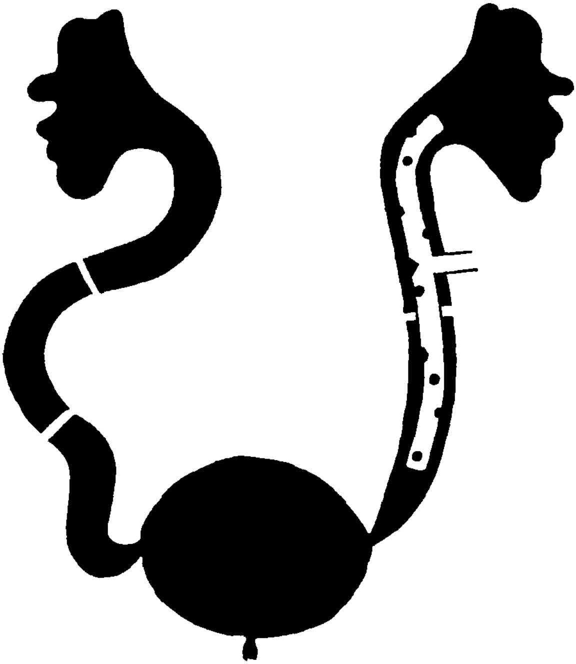

FIG 1 Schematic representation of resection of portion of redundant ureter and T-tube ureterostomy

so that transurethral correction of a bladder neck obstruction was impossible, at least until the child had grown a bit

I am well aware of the possibility that some of these children may have both a bladder neck obstruction and a concomitant stenosis of some portion of the lower ureteral segment and that this latter problem will require more than just a ureterostomy preliminary to bladder neck surgery

I dislike nephrostomy for two reasons 1) the fact that the procedure itself inevitably destroys some more nephrons when those units already may be pitifully few, and 2) because of the difficulty which there is in maintaining nephrostomy tube drainage for any length of time On the other hand, a T-tube placed in position properly with the upper arm of the T in the kidney pelvis, and the lower arm well down the ureter (fig 1) is not hard to insert and does not destroy additional kidney tissue at operation True, it cannot be replaced without more surgery, but oddly enough I have yet to see one become blocked from incrustations One did need replacing when a nurse cut off the tube flush with the skin in replacing a dressing In another case, the tube was found in the dressings about it one day without explanation

It has been interesting, even surprising, to see how well these little patients tolerated the T-tubes for long periods of time, as much as 8 months in one case Yet their removal always has been simple and in no case has drainage after removal lasted more than 13 days

It is a very satisfying experience to be able to limit one's activities to the cystoscopic removal of a bladder neck obstruction and at the completion of those activities clamp off both T-tubes, permit the urine to resume its normal course into the bladder and when, and only when, the child has proved his ability to empty his bladder completely, remove the T-tubes The ease of mind which accrues from knowing that the kidney situation is under mechanical control, through ureterostomy, while we strive to correct the bladder neck situation, is an important consideration

I submit, too, that in determining if a child's bladder neck obstruction has

TABLE 1 *Comparison of results by age on admission to hospital*

Age (yrs)	No of Cases	Possible Credits	Earned Credits	%
0–3	18	51	19	35
3–7	6	18	12	67
7–12	5	15	4	27

TABLE 2 *Comparison of results by procedure*

Group	No of Cases	Possible Credits	Earned Credits	%
1	6	18	5	28
2	16	48	20	42
3	8	24	16	67

* Group 1 Lower urinary tract drainage alone Group 2 Lower and upper urinary tract drainage Group 3 Chief reliance on ureterostomy

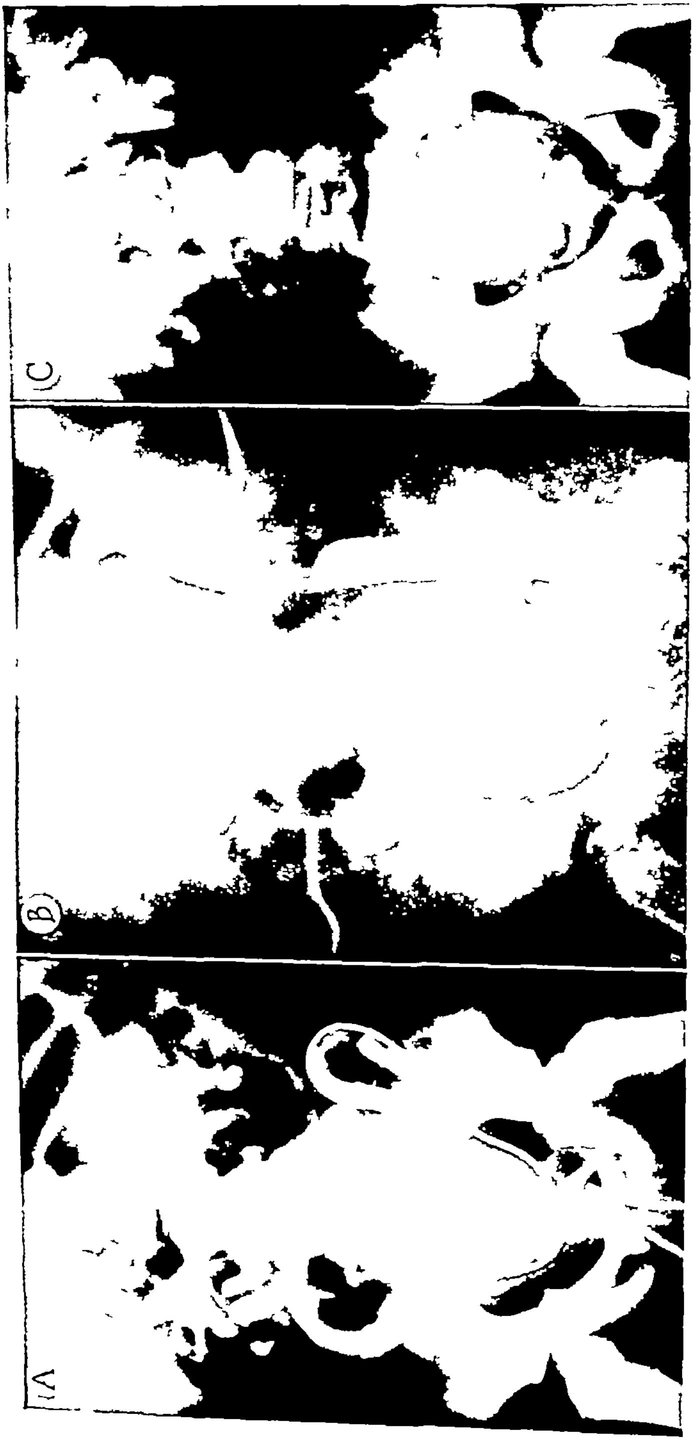

Fig 2 W F 1, preoperative urogram, aged 2, 1946 *B*, postoperative urogram 6 months later *C*, postoperative urogram, aged 9, 1953

been cured, the measurement of residual or absence of residual when urine has been permitted to accumulate in an intact bladder after clamping off the T tubes in both ureters offers more assurance that the boy really can empty his bladder than does the decision to close a cystostomy wound after cystoscopic inspection of the bladder neck This will always be so as long as the personal equation enters into the estimation of the patency of a child's vesical orifice

I regret that limitations of space do not permit inclusion of brief case abstracts on each of these 29 boys because I believe they present a more convincing picture of what has transpired than any chart of results would afford However, in an attempt to offer a comparison of results I have graded the individuals as follows

Grade A (3 credits) *Able to do what others of the same age can do without evidence of trouble or in need of any medical care*

Grade B (2 credits) Same as grade A, except that there are findings which require periodic evaluation and care

Grade C (1 credit) Still in enough trouble to require systematic urologic and pediatric care

Grade D (0 credit) An obviously poor prognosis

Grade E (0 credit) Patient is dead

Table 1 shows a comparison of results, using this plan of grading, for the entire group according to the age of the patient on admission to the hospital and without regard for the type of surgical management employed It would appear that the patient who has survived 3 to 7 years of life has perhaps the best chance

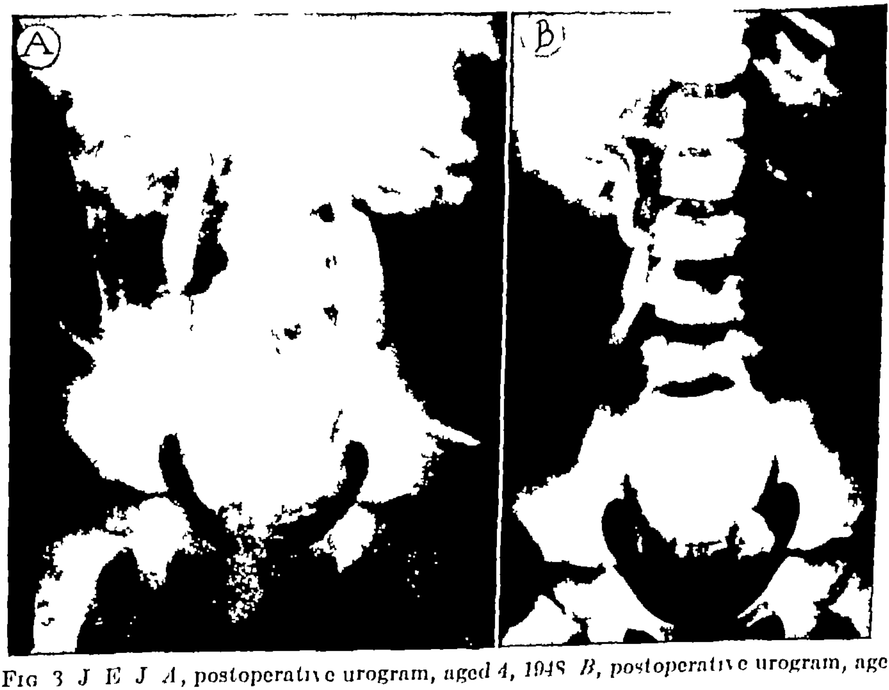

FIG 3 J E J *A*, postoperative urogram, aged 4, 1948 *B*, postoperative urogram, aged 6 1950

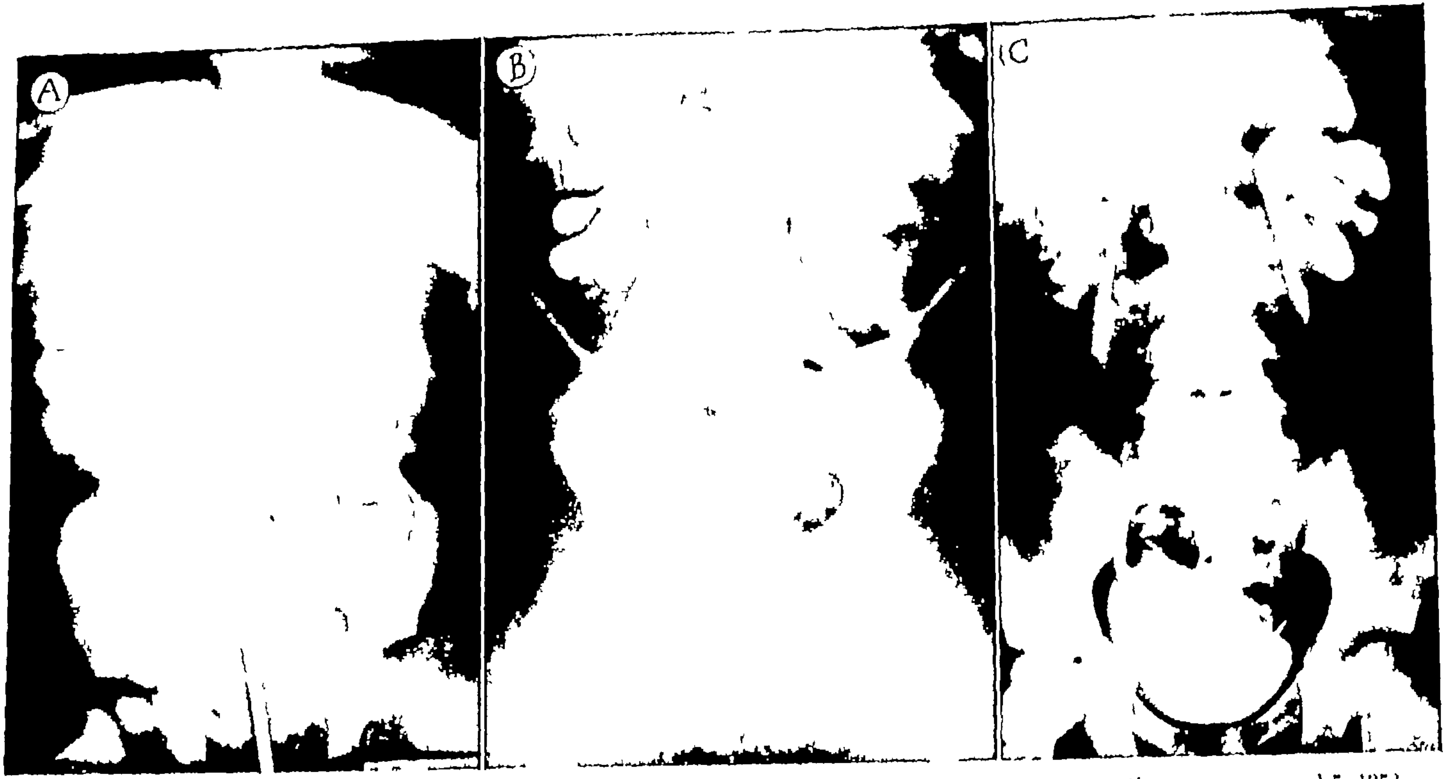

Fig 1 N H *A*, preoperative urogram, aged 1, 1949 *B*, postoperative urogram 1 month later *C*, postoperative urogram, aged 5, 1953

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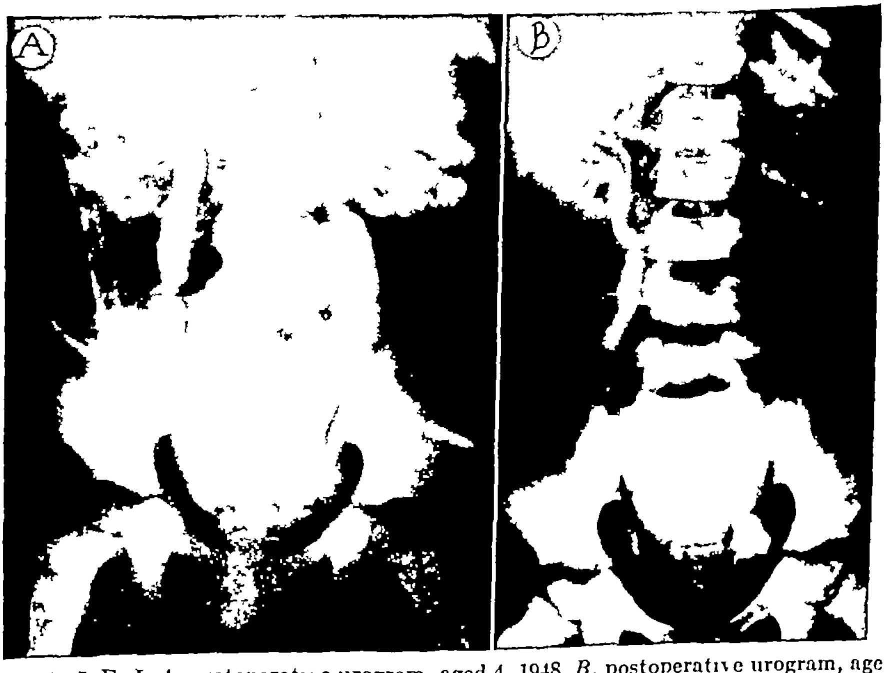

FIG 3 J E J *A*, postoperative urogram, aged 4, 1948 *B*, postoperative urogram, aged 6 1950

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GRANULOMA OF THE BLADDER ASSOCIATED WITH REGIONAL ENTERITIS: CASE REPORT

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It is well recognized that external, internal or multiple fistulas occur in approximately 50 per cent of the cases of regional enteritis. Ileovesical fistulas comprise approximately 5 per cent of these and apparently are incidental findings in cases presenting gastrointestinal symptoms; for a review of the literature disclosed only one case in which a diagnosis was made of this primary lesion after investigation of the presenting symptoms of urinary tract disease. The details of that case are not given. The case reported in our paper is illustrative in that the diagnosis of the underlying disease process was established when an ileovesical fistula was recognized during an extensive urological workup.

CASE REPORT

A 21-year-old single white female secretary was admitted for the first time June 6, 1955 with a history dating back to 10 months prior to admission when she noted the onset of a stomach ache that was a dull, vague, para-umbilical pain which persisted. Four months later, in addition to persistent stomach ache, the patient's temperature varied between 99 to 100F and she was weak and noted easy fatigue. The abdominal pain was not related to eating, straining at stool or urination. A complete workup including a gastrointestinal series revealed no disease. A diagnosis of neuritis was made and the patient received phenobarbital. Five months prior to admission the patient noted blood spots on the toilet tissue after urination. One month later she noted the onset of hematuria with coloring of the toilet bowl on two occasions. Cystoscopy showed a bladder infection that was treated unsuccessfully by aureomycin, achromycin, gantrisin, furadantin and finally penicillin. For the week prior to admission the patient noted bloody urine on several occasions, pain in the right lower quadrant upon urination, burning on urination and marked frequency.

Past history showed the usual childhood diseases and no adult illnesses. There was no history of nephritis or rheumatic fever. The patient underwent tonsillectomy at the age of 6 years and rhinoplasty at the age of 18.

Review of systems included the rhinoplasty 3 years ago, the stomach aches as described, some nausea, no vomiting and occasional diarrhea over the past 10 months as listed in the present illness. Urinary symptoms were as described on admission. The patient had never had peripheral edema. However, 4 years ago her face was puffy for a brief time and no known cause was found; no urinary symptoms were noted at that time.

The physical examination was completely within normal limits. The blood pressure was 120/80, pulse 88. Laboratory findings showed negative serology,

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for remedial care whereas the very young or the somewhat older child's chances are not as good

Table 2 represents a grouping by procedure, the outstanding feature of which seems to be that correction of the bladder neck obstruction by transurethral means associated with ureterostomy drainage of the upper urinary tract has given us better results than other methods

I know of no case in this series in which at the conclusion of our efforts there was complete return to normal architecture of either kidney pelvis or ureter This fact alone should stimulate additional effort to detect the condition as early as possible and cause us to redouble our efforts to devise better techniques for restoring the dilated structures to normal

The decision as to which child can be cured by surgery of the bladder neck alone is recognized as a difficult one—and there is no substitute for the exercise of careful clinical judgment on the part of the physician who is responsible for the child's care Moreover, the substitution of T-tube drainage in the upper ureter for nephrostomy and resection of redundant portions of the elongated ureter (fig 1) to help eliminate stasis in some cases are surgical devices which have meaning only insofar as they simplify or improve mechanical drainage The important consideration is that we recognize or, better still, anticipate renal damage, plan a continuing and logical reconstructive surgery of the child's urinary tract, employ all of the adjuvant therapeutic devices available, and try even harder than we have to restore more of these invalids to health

Representative cases are illustrated in figures 2, 3 and 4

CONCLUSIONS

Bilateral pyeloureterectasis in children due to congenital bladder neck obstruction is predominant in, if not limited to, the male sex

Chronic pyelonephritis was the chief complication of congenital bladder neck obstruction rather than pyeloureterectasis in the girls of this series where there were significant upper urinary tract changes

Most of our cases were under 3 years of age when first seen

Drainage at the upper urinary tract level carries a better prognosis than drainage confined to the bladder

Ureterostomy was attended by better results in this group than were the other methods

T-tube ureterostomy is a simple and efficient method to provide upper urinary tract drainage which merits further trial in these children

The author wishes to express his appreciation to the other members of the urologic and pediatric departments of the St Louis Children's Hospital for their co-operation in the compilation of these data, but also wishes to make clear that the opinions expressed herein are not necessarily shared by them

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was removed on the ninth postoperative day The patient was discharged on the eleventh postoperative day

Pathology report A thick circular portion of bladder wall measured 3 by $2\frac{1}{2}$ by $1\frac{1}{2}$ cm One surface was red and velvety and represented the bladder mucosa At the center, surrounded by papillary folds of congested mucosa was a dimple representing the entrance into the bladder of a sinus tract A probe passed through this tract to the opposite surface of the specimen which was composed of scar tissue representing the adhesions binding the bladder and small bowel together Also received were two segments of bowel each measuring 20 cm in length One segment was not remarkable grossly The other 16 cm from the ileocecal junction was abruptly thickened and indurated the wall of the bowel measuring 7 mm in diameter In this area loops of bowel were matted together and at one point near the mesenteric border a hyperemic area was noted A probe could be

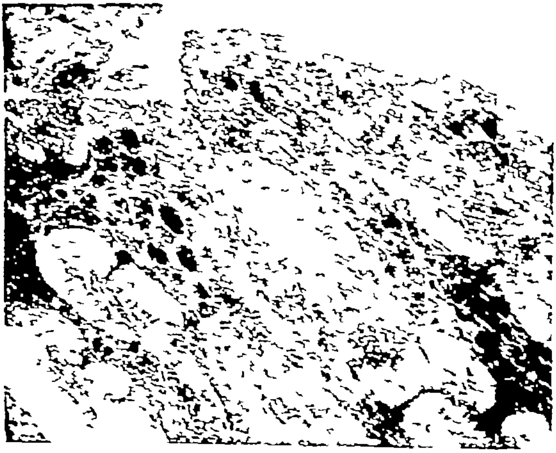

Fig 2 Inflammatory papilloma surrounds entrance of sinus tract in bladder × 190

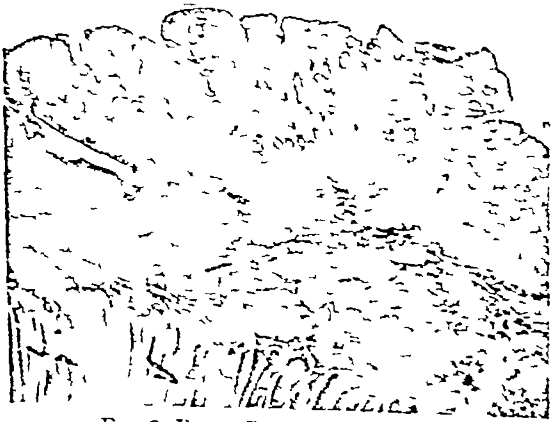

Fig 3 Ileum Regional ileitis × 17

O + blood group, hemoglobin 12 3 gm , white blood count 13,500 with 64 per cent polymorphonuclears The urine was tan and cloudy, it contained 4 plus albumin and was loaded with red and white cells The nonprotein nitrogen was 30, the fasting blood sugar was 54 Urine culture revealed E coli and alpha streptococci very sensitive to achromycin and aureomycin and terramycin X-ray examination of the chest was negative No gross lesion of the base of the bladder was seen on x-ray However, a mass was present in the dome of the bladder with minimal irregularities along the superior portion

Cystoscopic examination revealed a tumor on the dome of the bladder A biopsy disclosed only acute inflammatory reaction in the bladder mucosa

The patient underwent operation on June 10 Through a midline lower abdominal incision the bladder was opened A firm tumor was found in the fundus of the bladder which was firmly adherent to the peritoneum and to a similar inflammatory mass in the distal ileum and cecum The ileum was firm, the mesentery loaded with large, rubbery lymph nodes A partial cystectomy removed the involved dome of the bladder, the involved portion of the intestines was resected removing the distal two feet of ileum and the entire cecum and ascending colon An ileotransverse colostomy was performed Achromycin (500 mg) was left in the abdominal cavity, and a Penrose drain inserted into the space of Retzius The patient received one pint of blood and withstood the procedure well

Postoperatively, generalized urticaria was noted and this was treated successfully with benadryl The Levine tube was left in place 4 days and the patient maintained on parenteral fluids The bladder urine was completely clear by the third postoperative day By the fifth postoperative day the patient was passing gas freely per rectum, the achromycin was discontinued and the patient started on gantrisin ½ gm 4 times daily The patient was out of bed without complaints, the sutures were removed on the sixth postoperative day Urinalysis at this time showed 1 plus albumin with rare crenated red blood cells The bladder catheter

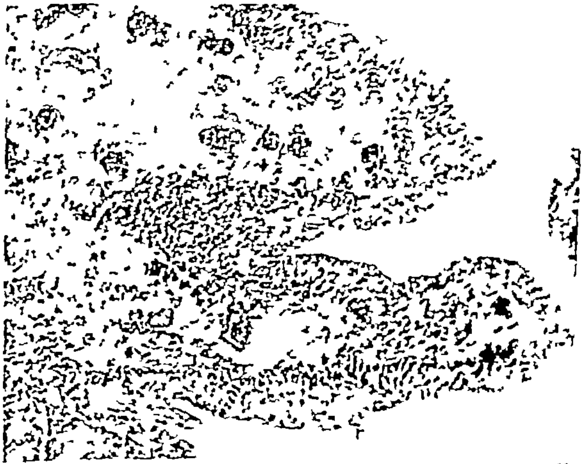

FIG 1 Biopsy of lesion in dome of bladder Inflammatory papilloma × 190

The finding of a granulomatous tumor of the bladder in a patient presenting even a vague history of unexplained diarrhea should prompt vigorous and repeated attempts to visualize the possible intestinal counterpart Regional enteritis must be considered in the differential diagnosis of urinary tract diseases

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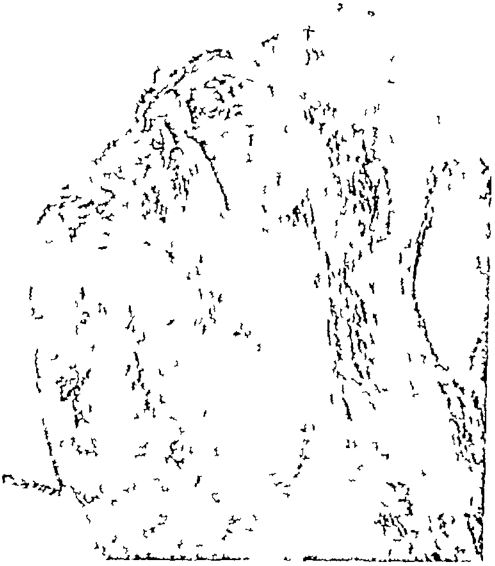

FIG 4 Ileum Sinus tract can be seen running through section from upper left × 18

passed without difficulty from this point in the mesentery into the lumen of the ileum The mucosa of the ileum was congested and edematous with superficial erosions

Microscopically the gross impression of regional ileitis was confirmed (figs 1 2, 3, 4)

COMMENT

This case illustrates the fact that nonspecific granulomatous tumor of the bladder may be due to vesical involvement in an extensive regional enteritis accompanied, in this case, by an ileovesical fistula It is of interest to note that of 42 cases diagnosed as regional enteritis at the New Haven Hospital since 1940, no cases of ileovesical fistula have occurred However, one patient who had urinary symptoms was found to have a rectovesical fistula as a result of diverticulosis, a similar picture was seen in a case of endometriosis involving the small bowel

Noteworthy points in this case are 1) the repeated failure to establish a diagnosis by conventional means, 2) the erroneous and harmful labeling of the patient as a neurotic, 3) the final establishment of the diagnosis by persistent and systematic investigation of the unusual urinary symptoms

SUMMARY

A case of regional enteritis with ileovesical fistula is presented, in which the true diagnosis was made only after investigation of the presenting complaints of urinary tract infection which was due to a granulomatous lesion of the dome of the bladder as a result of involvement with fistula formation in an extensive regional enteritis

The finding of a granulomatous tumor of the bladder in a patient presenting even a vague history of unexplained diarrhea should prompt vigorous and repeated attempts to visualize the possible intestinal counterpart Regional enteritis must be considered in the differential diagnosis of urinary tract diseases

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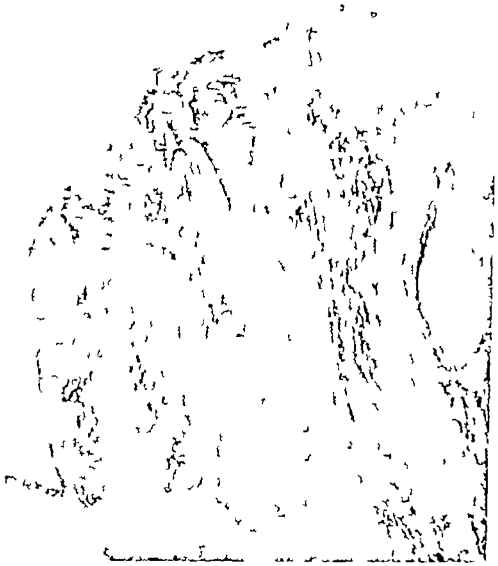

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BLADDER POUCH FOR PROLONGED TUBELESS CYSTOSTOMY

BERGET H BLOCKSOM, JR

This paper is based on the thought that there are indications for unimpeded drainage of the bladder, permanent or prolonged—a simple procedure that could be used in patients who are poor risks and in those in whom urinary diversion without cystectomy is contemplated Recourse, heretofore, has involved use of catheters with all the inherent complications of infection, incrustation, bladder spasms, pain, etc

The procedure I am about to describe can almost be gleaned from the title and will hence require but little elucidation A midline incision is made commencing about three finger-breadths above the symphysis pubis and extended upward for a distance of 6–7 cm The rectus sheath is cut in a similar manner and the anterior surface of the bladder exposed After reflecting the peritoneum cephalad the bladder is entered through a high stab incision, unless, as in our case, there was already a pre-existing cystostomy hole which had accommodated a dePezzer catheter With the index finger inserted into the bladder, further mobilization and elevation of the bladder are accomplished until it can be drawn well up into the wound in an area of the abdominal wall that is smooth and would be devoid of folds if the patient were to assume the sitting position The walls of the bladder are then sutured to the rectus sheath with absorbable sutures and the skin edges in the vicinity of the marsupialized bladder are drawn down to the bladder walls and rectus sheath with similar sutures to provide an abundance of redundant bladder protruding from the wound Closure is completed with a few heavy dermal sutures embracing all layers of the remaining defect in the abdominal wound The cystostomy thus prepared should admit the index finger very easily Sump drainage may then be provided for the patient's comfort while the wound is healing but this is not essential

CASE REPORT

The patient, a 75-year-old white man, had been treated many years for urethral stricture He also had a rather large adenomatous prostate without severe symptoms of prostatism although a prostatectomy had been considered The urine was essentially clear In December 1954 the patient complained of pain in the perineum and hard, fibrotic tissue could be felt in the location of the perineal urethra He was put on cortisone for a few days following which a 24F sound was easily passed, however, the patient was unable to void afterwards and had to be admitted to the hospital and placed on urethral retention catheter drainage The diagnosis of possible carcinoma of the urethra was entertained and on December 22, 1954, under spinal anesthesia, a 24F McCarthy resectoscope was introduced Inspection of the bladder and prostatic urethra showed 3 plus trabeculation with cellule formation and a large trilobar hypertrophy of the bladder About 3 cm distal to the external sphincter there was an area of nar-

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Read at annual meeting of South Central Section of American Urological Association Mexico City October 28–November 1, 1956 rowing with disrupted urethral mucosa corresponding to the area of palpable hardness in the perineum A generous piece of hard, rubbery tissue was then resected from this area

In spite of the belief that a representative biopsy had been obtained the pathological report was negative for carcinoma Following this procedure the patient was unable to void after removal of the urethral catheter On January 4, 1955 a punch cystostomy was done and the patient sent home with a suprapubic catheter in place

During the next month the mass in the perineum failed to recede in spite of diversion of the urinary stream, so he was readmitted to the hospital On February 7, 1955 an open biopsy was taken the pathological report was squamous cell carcinoma On February 10, 1955 a total penisectomy, carried down to triangular ligament was performed The wound was closed around an indwelling Foley catheter which had to be soon removed because of intolerable bladder spasms We were forced thereafter to rely on drainage by way of the suprapubic punch cystostomy which also was to cause much trouble in terms of recurrent episodes of bladder spasms calcification and finally bladder calculi in spite of every preventive measure

We persisted in following the patient and put up with numerous calls of complaints relative to the catheter for the next 17 months chiefly because we took a dim view of his prognosis and of accomplishing further operative procedures In June 1956 we decided that there was no discernible recurrence of the carcinoma and that he possibly had non-x-ray-opaque bladder calculi He was readmitted to the hospital the bladder was explored and one large bladder calculus was removed in addition to a collection of gravel in the prostatic urethra The bladder was marsupialized as heretofore described

COMMENT

I have been unable to find a report of this procedure in the literature and the present editor of the YEARBOOK OF UROLOGY, Dr William Wallace Scott, assures me there has been none in the 6 years of his tenure of office

I am not unmindful of Peyton and Headstream's recent report of construction of a perineal urethra with a skin graft technique In our case however the patient would have had to have a preliminary prostatectomy for which he was neither physically nor psychically a candidate The procedure we are describing seemed a nearly ideal way out of a dilemma

We had considered other ways of diverting the urine all of which would have required more extensive surgery Any method which leaves an intact bladder in place without drainage is contraindicated We have observed an example of this where a general surgeon from another city performed a Bricker pouch operation because of incontinence and neurogenic bladder supposedly due to spina bifida We were consulted because the patient had been having recurrent chills and fever over a period of 2 years Insertion of a catheter through the normal urethra into the intact bladder produced a gush of extremely foul pus thereafter the patient was instructed in the care of herself to prevent further such episodes

I am led to speculate on other indications for this procedure Persistent encrusted cystitis, from whatever cause, might be an indication It would seem to me to be highly suitable also for some cases of neurogenic bladder, especially if dilated ureters with reflux are present and constant unimpeded drainage would be better than reconstituted near-normal micturition which might be achieved by other means

We have observed a case recently in an infant where there was a very thick walled bladder apparently due to partial bladder neck obstruction The bladder itself contained no residual urine but the ureters were enormous and the urine,

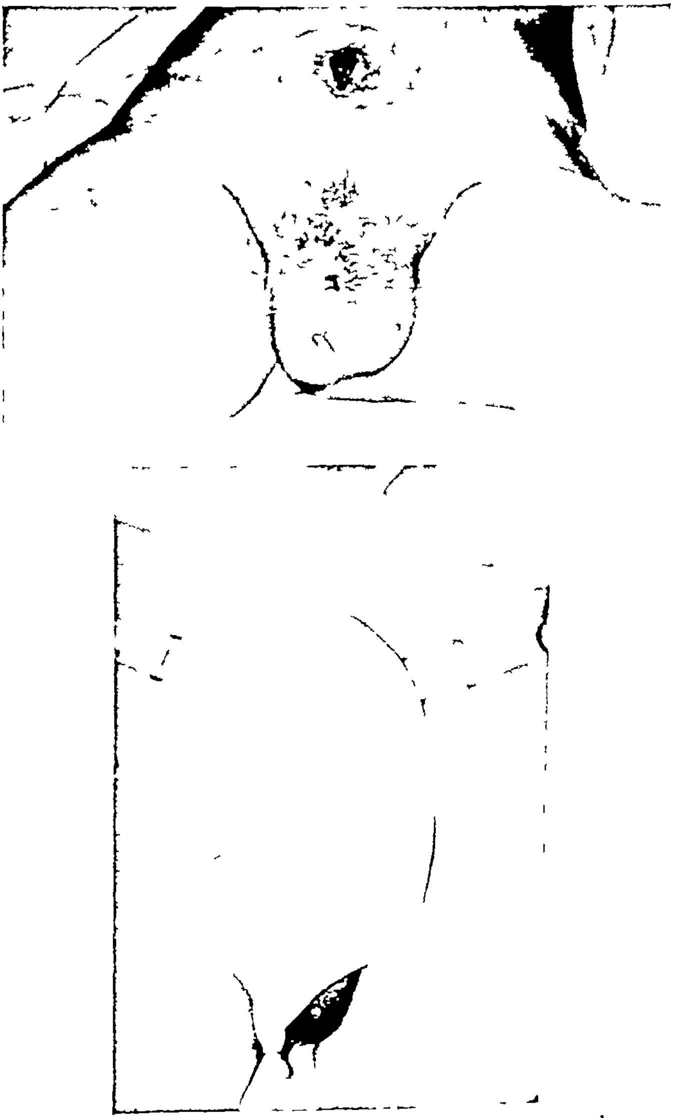

FIG 1 Two weeks postoperatively and with temporary bag

taking the lines of least resistance continued to stretch the ureters This case requires continual uninterrupted drainage to cause shrinkage of the ureters before tackling the bladder neck obstruction I don t believe intermittent micturition, if it could be obtained prior to shrinkage of the ureters would suffice because the bladder at best would be an almost rigid undistensible conduit and the thin ureteral walls would have to act as the detrusor In such a case a large suprapubic catheter might suffice but considering the potentiality of catheters to cause foreign bodies the bladder pouch on a prolonged though temporary basis would in my opinion be better Since the infant is still in the wetting stage no prosthetic appliance would be needed The procedure used in such a case as this obviously must be one that can be reversed at any time much as a loop colostomy can be repaired and an intact colon reconstituted Its limitations need exploring obesity may be a contraindication and the operation might prove to be difficult on a severely contracted bladder However it should be emphasized that our patient with the urethral carcinoma had a considerable degree of contraction after 1½ years of constant suprapubic drainage

Our patient has had no bladder spasms since operation carries no residual urine and so far has formed no stones His bladder and even his prostatic urethra can be explored digitally without anesthesia The greatest difficulty has been teaching him and his family to cement the bag properly but success seems assured in this regard as he has gone more than three days without the bag coming off and in any event, this is an individual problem

In this connection there is need for a better prosthetic appliance—one that has a more flexible rim to be cemented to the skin so that it will not tend to pop off when the contour of the skin changes with the position of the body Even as it is we are happier to be spared constant telephone calls office calls and multitude of complaints we endured the many months the patient wore the catheter

SUMMARY

A simple method of using the bladder as a pouch for tubeless diversion of the urine has been presented

An illustrative case has been presented

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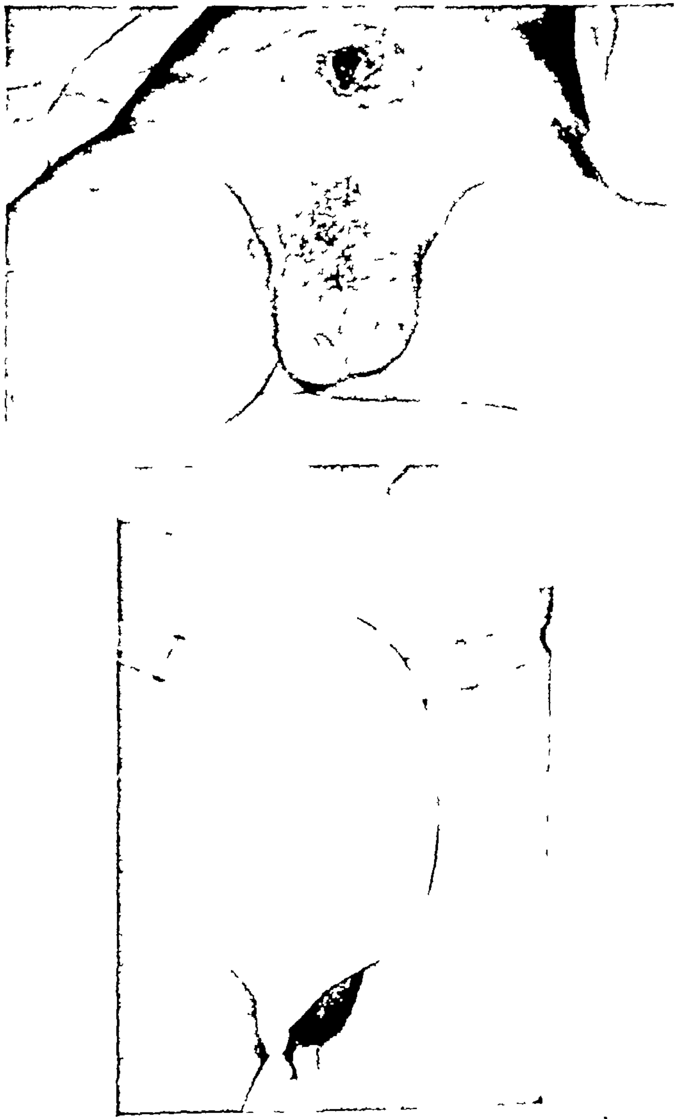

FIG 1 Two weeks postoperatively and with temporary bag

Diagnostic procedures commonly accomplished in cases of suspected bladder cancer need not be reviewed here In this regard Jewett has cited the need for careful bimanual examination under anesthesia so that superficial or deep infiltration can be recognized Choice of treatment of urinary bladder cancer hinges to a great extent on the presence or absence of infiltration and on the degree of infiltration if such is present There is a high percentage of vascular invasion in tumors infiltrating the muscularis or beyond[9] Recent work by Baker and colleagues[10] indicates a possibility that even with superficial bladder tumors there may be involvement of a considerable portion of the bladder lymphatics without cystoscopic evidence There may even be lymph node involvement

The present status of the treatment of bladder cancer has been well put by Marshall,[7] who states that "While awaiting some chemotherapeutic solution to the problem of bladder tumors, specifically bladder cancers, or some understanding of their pathogenesis that might assure their prevention, urologists have to treat patients by the means at their disposal, though these means may appear inadequate" Radiation therapy is one of the means at our disposal for treating bladder cancer

Many different methods of radiation have been used These include external radiation, interstitial radiation with radon, radium and radioactive isotopes, intracavitary radiation with solid and liquid radioactive materials, and intracavitary radiation with contact therapy apparatus at surgery (Chaoul apparatus)

As so called supervoltage therapy apparatus was developed and put into use, reports in the literature indicated that this form of external radiation might improve the results of therapy in cases of bladder cancer over that obtained with conventional radiation therapy (200–250 kvp range) About three years ago we obtained a cobalt 60 teletherapy unit and decided to treat some cases of bladder cancer with this unit in order to study the effectiveness of this type of radiation therapy

The cobalt 60 unit used is a theratron model B manufactured by the AEC of Canada Limited, Ottawa, Canada (fig 1) The radiation from this unit is equivalent to that obtained from a 3 MEV x-ray therapy apparatus Briefly, it has all of the advantages of supervoltage x-ray, including increased depth dose, decreased skin reaction, a decreased integral dose which leads to better toleration of the radiation by the patient and decreased selective absorption in bone With this apparatus, because of its mechanics and the absence of cables, precision rotation of the radioactive source about the patient is possible

All cases here reported were treated with this unit utilizing full rotational technique The axis of rotation is the center of the urinary bladder The method used for localization of this point is as follows The bladder is filled with opaque contrast medium The patient is placed on the radiographic table in the supine

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COBALT-60 TELETHERAPY FOR URINARY BLADDER CARCINOMA TWO AND ONE HALF YEARS' EXPERIENCE

L E PLANK, J W GROSSMAN AND S D CAMPANELLA

Urinary bladder cancer continues as the most important malignancy of the urinary organs[1] The death rate from bladder cancer is 3 2 per cent of the total deaths from malignant disease The etiology of the disease remains obscure Certain chemical compounds, benzidine and beta nepthylamine, are responsible for the formation of occupational tumors[2 3 4] Some work indicates that in the general population a defect in the metabolism of tryptophan in certain individuals may cause them to develop bladder cancer[5]

Practically all tumors of the urinary bladder are epithelial in origin They occur principally in adult life and about two males are struck with the disease for every female The important factors in prognosis are the degree of malignancy and the depth of infiltration, as established by Jewett[6] These two factors are closely linked, and as a rule low grade carcinomas are encountered in superficial stages of penetration and the more malignant carcinomas in deep stages of penetration So close is this association that if one encounters a bladder cancer which histologically is highly malignant, but which appears to be superficial, an upward revision of the degree of penetration should be considered[7]

The more favorable outlook for the patient with malignant papilloma or infiltrating carcinoma with superficial penetration as compared to the unfortunate individual upon whom a diagnosis is made only after there is deep muscular penetration, frequently associated with perivesical extension or metastasis, seems well established Results of studies following cystectomy reveal that tumors infiltrating less than half way through the muscularis are usually still confined to the bladder wall and without metastases, indicating that the frequency of lymph node metastasis is probably closely related to the depth of penetration of the tumor The degree of tumor infiltration is reflected somewhat by the duration of symptoms manifested chiefly as hematuria and vesical irritability with or without pyuria Hematuria and vesical irritability of some duration frequently, but of course not absolutely, indicate infiltration[8]

Read at annual meeting of South Central Section of American Urological Association, Mexico City, October 28–November 1, 1956

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FIG 2 a Method of obtaining anterior-posterior localization radiographs of urinary bladder Lead marker strip is in position on abdomen with patient supine Ink marks are made on patient's skin corresponding to lead strips b Set-up for lateral view Upright lucite rods with lead strip at each end [illegible] are shown X-ray beam is directed transversely across table

ions or transient radiation sickness It usually takes six to seven weeks to deliver a tumor dose of 5 000 r and seven to nine weeks to deliver a tumor dose of 7 000 r The field size varies from 10 by 10 cm to 15 by 15 cm

The entire bladder was treated in all cases An isodose chart showing the distribution of radiation for a 10 by 10 cm portal is shown in figure 4 The 10 by 10 cm portal was used where from available data it seemed that the tumor was confined to the immediate bladder area No larger portal than 15 by 15 cm was used where spread beyond the bladder and lymph node metastases were suspected At times the size of the bladder as seen in the localization cystogram determined the size of the portal

Radiation therapy administered in less than lethal doses can alter tumor stroma such that subsequent radiation therapy administered by whatever means may fail to produce even good palliative results In the series of cases reported those patients with previous radiation therapy did poorly Tumor stroma is of great importance in radiation therapy This stroma can be adversely altered by infection so as to actually frustrate successful treatment It is therefore important to control infection as much as possible prior to the start of radiation therapy [7]

The patients in this series were referred by a number of urologists for treatment No one who has not actually done so can appreciate the difficulty of assembling essential data in such a situation It became readily apparent that the only common meeting ground for grading these tumors was a study of biopsy material Following therapy accurate cystoscopic and microscopic followups were obtained at varying intervals after completion of therapy (table 1)

With exception of one case with a 5-month followup all patients presently being followed completed therapy at least a year before these cases were charted Twenty-three patients completed the therapy Of these 7 patients died of the disease the earliest 3 months after completion of therapy One died of cardiac failure 10 months after therapy with residual tumor and one died in 8 months in uremia with residual tumor One patient died accidentally and no autopsy

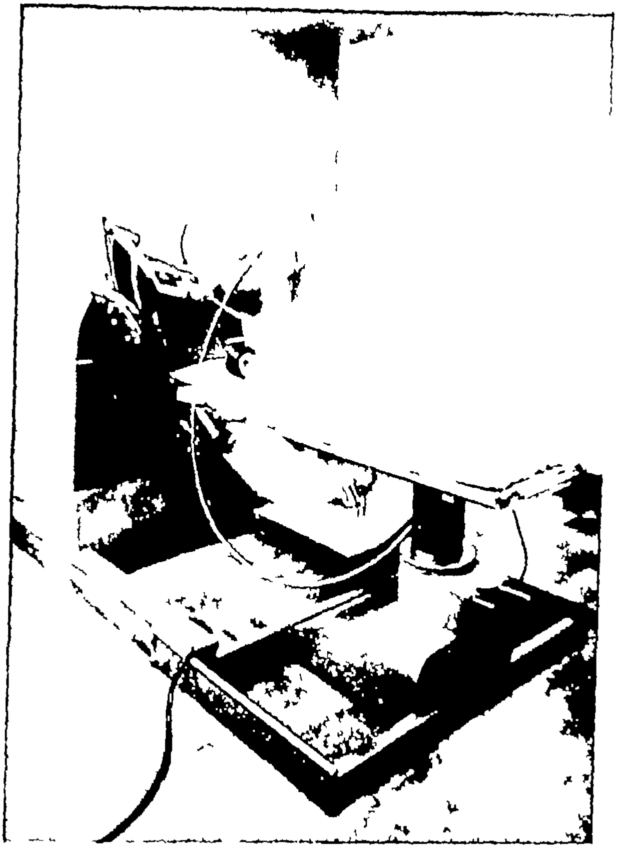
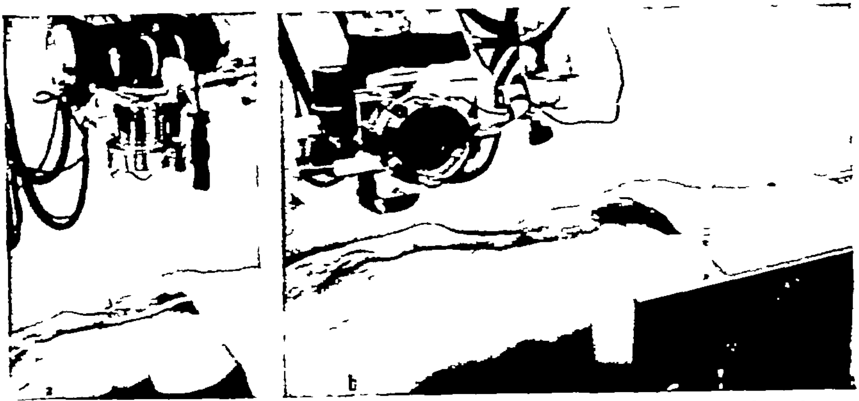


FIG. 1. Theratron B cobalt 60 teletherapy unit. Patient in position on treatment couch. Path of rotation of radioactive source around patient is indicated by white circle.

position exactly as he is to be placed for the actual treatment. An anterior-posterior and a lateral radiograph, with the central beam horizontal, are made of the urinary bladder. For the anterior-posterior film a marker made of lead strips is fastened to the patient's abdomen with adhesive tape, and the position of the strips painted on the skin with ink (fig. 2, *A*). For the lateral view two upright markers with lead strips 1 cm. apart are used, one in contact with each lateral aspect of the pelvis (fig. 2, *B*).

From these films the center of the bladder is determined in two planes. On the lateral films the depth of the center of the bladder above the table top is measured. The intersection of a line projected downward from the anterior skin marker over the bladder midline with the proper depth point is the center of the bladder and the axis of rotation (fig. 3, *A* and *B*).

A constant tumor source distance of 75 cm. was used in all cases. Complete rotation was employed with the source moving about the patient at a speed of one revolution per minute. Most patients were treated 5 days a week, with an average daily tumor dose of 200 r. During the course of the treatment short periods of rest of several days are required because of resultant cystitis, proc-



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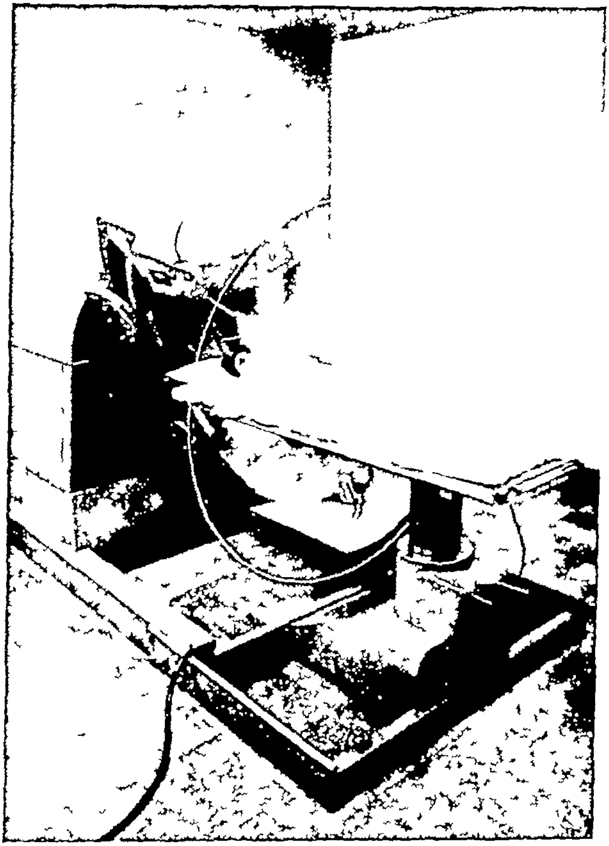

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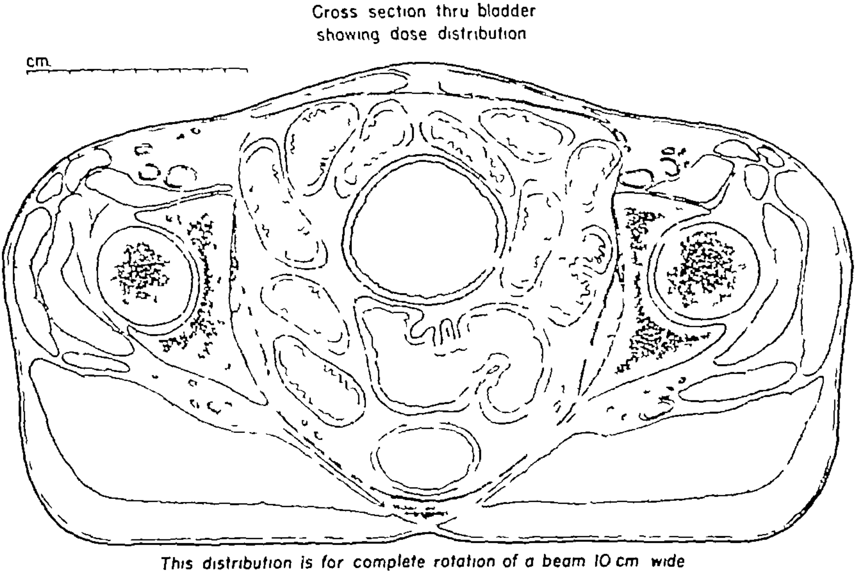
Cross section thru bladder
showing dose distribution
cm
This distribution is for complete rotation of a beam 10 cm wide

FIG 4 An isodose chart showing dose distribution across section of pelvis through center of urinary bladder for a Co^{60} beam, 10 cm wide, utilizing complete rotation with center of axis of rotation 75 cm from source

of note in any of the patients In one patient who had previous conventional radiation and a suprapubic cystostomy prior to cobalt treatment, a suprapubic fistula developed after cobalt therapy before he died as a result of tumor Proctitis developed in only two patients Both of these died as a result of bladder cancer No patient who is living has rectal symptoms The patient who presently has an equivocal biopsy has a limited bladder capacity of 30 cc The patient who has a persistently positive biopsy had a bladder capacity of 75 cc 6 months after completion of treatment, it is now 200 cc Only one patient clinically free of disease has a small bladder, it holds 100 cc An 80-year-old woman who had grade 2 carcinoma involving the entire bladder floor had a limited bladder capacity following cobalt therapy and bilateral hydronephrosis developed Presently, 30 months after treatment, her bladder capacity is 300 cc, the hydronephrosis has disappeared and the bladder is clear cystoscopically and the previous tumor-bearing area has given repeatedly negative biopsies Slightly over half of the cases treated were placed on cortisone therapy while receiving their radiation No conclusions can be drawn, but the impression is that the cortisone patients did better in general and developed less bladder contracture

This series is presently small It would appear, however, that in most cases there is little possibility of curing otherwise hopeless urinary bladder cancer Several cases lend encouragement, however That of the 69-year-old man with 38 previous transurethral resections, a bladder full of tumor and with little alternative but cystectomy, and that of the 80-year-old woman with extensive, grade 2 cancer from whom 40 gm of tumor was resected, and who could not have possibly withstood cystectomy Both of these patients are alive and with-

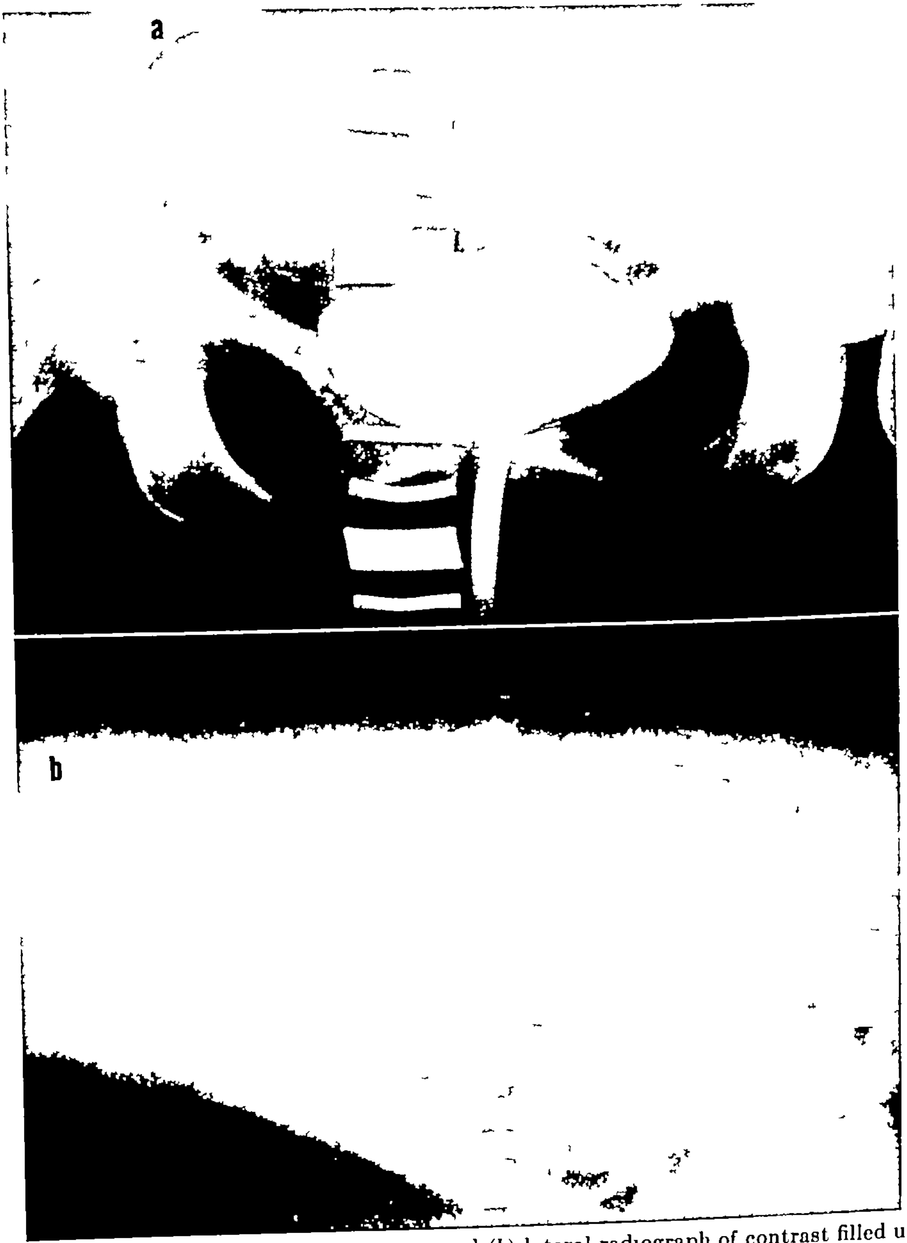

Fig 3 Resulting (*a*) anterior posterior and (*b*) lateral radiograph of contrast filled urinary bladder Position of center of bladder on the anterior posterior view is easily correlated with skin mark corresponding to lead marker at same level as center of bladder On lateral view position of center of bladder above table top is found by projecting center of bladder X to each marker and taking mean of two readings

was obtained In one case there is persistently positive biopsy proof of cancer and in one other the biopsy is equivocal The remaining 11 patients are negative, cystoscopically, and some by biopsy where tissue pieces were taken of suspicious lesions or in a previous tumor-bearing area There were no skin reactions worthy out evidence of tumor 2½ years after completion of therapy This would seem to indicate that even some fairly extensive tumors are radiosensitive This possibility of a favorable response and hope for a decreased percentage of recurrence of superficial tumors, because of destruction by radiation of independent foci that are not readily evident for treatment by other means, must be kept in mind

Certainly there is no argument against radical surgery in suitable cases of urinary bladder carcinoma where surgery is considered curative

Therapy as outlined here, is considered a suitable palliative instrument where needed, and one wonders if time may not prove the worth of its use in cases treated by conservative surgery as a prophylaxis against subsequent tumor recurrence with dire consequences

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TABLE 1—*Summary of urinary bladder carcinoma cases treated with cobalt-60 rotational beam teletherapy, January 1954 to July 1956*

Age Sex	Tumor Grade	Dosage R, Days Completed	Post Cobalt Cysto	Post Cobalt Biopsy	Signs	Symptoms	Results
80 F	TC 2	5800 37 2–54	Neg	Neg	Early BC now 300 cc	Noct 2 times	Good
69 M	TC 2, extensive	7109 46 4–54	Neg	Neg	0	0	Good
57 M	TC 1	7000 56 7–54	Neg	Neg	0	0	Good
58 M	TC 1, sessile	8040 56 8–54	Susp	Neg	BC 100 cc	Freq	Good
79 F	TC 2	6522 43 10–54	Neg	Neg	0	0	Good
57 M	TC 1	7603 51 11–54	Neg	Neg	0	0	Good
65 M	TC 2	7605 58 12–54	Neg	Neg	0	0	Good
74 M	TC 2	7500 43 12–54	Neg	Neg	Incont from TUR	Incont	Good
64 M	TC 1	6534 46 4–55	Neg	Neg	0	0	Good
62 M	TC 3	8000 58 7–55	Neg	—	0	0	Good
60 M	TC 2–3	7068 50 7–56	Neg	—	0	0	Good
Equivocal biopsy							
58 M†	TC 3	8000 59 7–55	Susp	Susp	BC 30 cc	Freq	Palliative
Persistent disease							
55 M	Sq cell 4	4590 39 1–54	Pos	—	Hematuria	Freq	Died 6–54, Ca
79 M*†	TC 4, adenoca	5238 40 6–54	—	—	Suprapubic fistula	Drainage	Died 1–56, Ca
59 M	TC 2	7489 47	Pos	Pos	BC 200 cc	Freq	Palliative
79 M†	TC 2	8000 56 8–54	Pos	Pos	0	0	Died 7–55, Cardiac failure
65 F	TC 3, exenter	7178 60 10–54	—	—	0	0	Died 9–55, Ca
64 M†	TC 4, extraves	7128 52 12–54	Pos	Pos	0	Freq	Died 10–55, Ca
53 M*	Sq cell 4	4047 33 12–54	Pos	—	Hemat pain BC 90 cc	Freq proctitis	Died 1–56, Ca
79 M	Undiff Ca	6290 47 6–55	Pos	—	0	0	Palliative
55 M	Anaplas TC extraves	8000 53 4–55	Pos	—	0	Freq	Died 7–55, Ca
57 F*	TC 2	4800 50 5–55	Pos	Pos	BC 120 cc	Freq proctitis	Died 3–56, Ca
49 M†	Sq cell extraves	6000 48 5–56	—	—	Hematuria fever	Freq	Died 8–56, uremia Ca

TC—Transitional cell, BC—Bladder contracture

* Previous radiation † Previous segmental resection

pitalization at Hughes Spalding Pavilion a tedious circumcision for obliterative balanoposthitis and an internal urethrotomy for dense strictures were done Cystoscopy was performed and was deemed technically unsatisfactory due to severe cystitis or extensive tumor formation Antibiotics were given for infection and on May 11 1956 another cystoscopy under local anesthesia in the office was interpreted as showing generalized bladder neoplasm The patient was admitted to the hospital and routine preparations made for cystectomy and bowel transplants using sulfathalidine The work of Bohne and associates had been noted and the following procedure was performed

Spinal anesthesia was administered With the patient supine the abdomen and genitalia were prepared and draped and a midline incision made from the symphysis pubis to the umbilicus Bleeders were clamped and ligated with 00 chromic catgut The rectus fascia was incised and the recti muscles separated Retracting the peritoneum superiorly blunt dissection was used to free the anterior and lateral sides of the bladder and prostate By placing transfixion sutures of No 1 chromic catgut in the puboprostatic vascular pedicle the prostatic urethra could be severed at the apex with minimal hemorrhage The prostate was then grasped on its free end with two Allis forceps and the remaining prostate and posterior bladder dissected carefully off the rectum The lateral vascular pedicles including the vasa deferentia were clamped in multiple series, divided and ligated with No 1 chromic catgut The ureters were cut about 1 5 cm above the bladder Then the entire specimen including the prostate bladder seminal vesicles parts of the vasa deferentia and parts of the lower ureters were removed in one mass No nodes were found but probable rectal fixation was present The lower ureters could be seen free in the empty pelvic cavity and by crossing in a straight line the ureters could be approximated to the cut posterior urethra without tension Then two 10F red rubber urethral catheters were inserted through the penile urethra about 15 cm projecting above the severed prostatic urethra and about 6 to 9 cm projecting beyond the meatus One catheter was threaded up one ureter and the other up the other ureter The ureters and posterior urethra were then approximated with two sutures of 00 chromic catgut The catheters were anchored to the penis by sutures to the glans and by adhesive tape A one-half inch Penrose drain was left in the space of Retzius and the wound closed with No 1 chromic catgut for the muscle and fascia and 3–0 black silk for the skin The operating time was 2 hours 1 pint of blood was used, the condition of the patient remained satisfactory

The pathological report was advanced adenocarcinoma involving the prostate bladder and seminal vesicles and extending through the line of excision

Postoperatively the urethral catheters were left indwelling for 3 weeks Moderate suprapubic drainage occurred for 10 days then ceased After removing the catheters the patient complained of marked frequency with precipitous voiding for about two weeks On June 15 1956 he was seen in the office and voided 3 ounces with good control and a normal stream ’ One month later the capacity was 10 ounces with only occasional enuresis Two months after cystectomy a cystogram revealed a large bladder and bilateral ureteral reflux A film made

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RADICAL CYSTECTOMY FOR ADVANCED CARCINOMA OF THE BLADDER

THOMAS J FLORENCE

Vesical cancers show tremendous individual variations The types of neoplasm, their sizes, locations and number, the depth of invasion present, the existence of local or distant metastases all these make no two cases alike as to treatment or prognosis In this discussion I would like to postulate that particular growth which might be cured or greatly helped by total cystectomy

Urine is formed continuously in the kidneys and only by the development of a suitable reservoir has man become a social animal To date this reservoir, the urinary bladder, has resisted "successful" imitation Therefore its removal is no trivial affair, making any but an aquatic existence precarious The immediate and chief problem is where to place the ureters Two methods are now in well established usage Skin ureterostomy may be done or some portion of the gastrointestinal tract can be used Both procedures are consistent with several years of fairly normal life and each deserves consideration if a serious disease can be cured or greatly ameliorated However certain major objections exist, such as ureteral obstruction, reabsorption of electrolytes, infection and inconvenience to the patient

For many reasons a more natural or physiologic solution has been desired Stimulated probably by the observation that the bladder has a remarkable regenerative power, partial cystectomy has been carried to the extreme in the experimental work of Bohne, Osborne and Hettle at the Henry Ford Hospital in Detroit They removed the entire bladder in dogs and obtained a regenerated pouch lined with transitional epithelium and containing smooth muscle in its wall Six to ten weeks were required for epithelization Smooth muscle was present at fourteen to sixteen weeks In one dog a section at 21 weeks showed ganglion cells and nerve tissue Functionally a number of the animals were continent and voided in a normal manner The longest survivor at the time of reporting was nine months Only 3 cases were described in detail and ureteral reflux was mentioned in two of these Technically the entire bladder was removed and a plastic mold inserted to serve as a framework for the future "bladder " Later a collapsible plastic bag with ureteral extensions was used This could be deflated and removed through the urethra The overall mortality and morbidity were high

CASE REPORT

A 44-year-old married Negro man was seen April 6, 1956 because of gross hematuria due possibly to excessive lifting on his job at a potato chip factory The urinalysis showed many blood cells, 2 plus albumin and no sugar Marked phimosis was present On rectal examination hardness and irregularity of the prostate and bladder region were felt with questionable fixation Preliminary intravenous urograms in the office demonstrated bilateral moderate hydronephrosis, ureteral dilatation, and a small, irregular bladder Ten days later during hos-

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Read at annual meeting of South Central Section of American Urological Association, Mexico City, October 28-November 1, 1956

immediately after voiding showed complete emptying with much drainage of the dilated pelves and ureters Intravenous urograms 2 days later demonstrated prompt and good function with little change in the hydronephrosis from that before surgery Hospitalization for further studies was done in September 1956 The blood urea nitrogen was 20 mg per cent A cystogram again showed bilateral reflux and some diminution in "bladder capacity " Investigative zeal prompted a probably unwise attempt at cystoscopy and biopsy of the new "bladder " The "bladder" wall appeared smooth and not unlike normal mucosa except in the floor where recurrent tumor was suspected At this point manipulation resulted in penetration of the superior wall with visualized entrance of a piece of greater omentum through the tear Cystoscopy was discontinued and a 20F Foley catheter inserted to keep the bladder empty for 10 days To our surprise no complications occurred At the present time the patient is living with cancer His general condition is fair The urine contains many pus cells and there have been two episodes of acute pyelonephritis which responded to penicillin and streptomycin A normal sensation to void developed 6 weeks after surgery

In assaying the worth of a new procedure one example is woefully inadequate Also any particular example might well be completely misleading However such was done and an attempt will be made to give a personal evaluation The method is attractive because of simplicity in execution and naturalness of results After removing the pathological process the operation is essentially over, certainly an advantage over surgery which incorporates bowel transplants The patient can still void in a normal manner and a closed urinary tract is preserved against invading micro-organisms Data are still necessary to determine whether such a simple procedure as was done in this case will suffice or whether an inflatable apparatus produces a better bladder The permanent vesical capacity and how often reflux will occur must be determined in human cases Also what effects this type of reflux will have on kidney function and if any method of correction can be done pose intriguing problems From the important standpoint of total removal of cancer I believe this method is as effective as any not involving removal of the rectum

In conclusion, a new operative procedure is reported It is technically feasible and probably workable However it is neither recommended nor condemned but merely presented in the hope that other urologists may by frequent usage establish its true place in the treatment of bladder cancer

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PRIMARY CARCINOMA OF THE MALE URETHRA REPORT OF A SEVEN-YEAR CURE BY RADICAL SURGICAL EXCISION

HARRY M SPENCE AND JOHN DENMAN

From the Urological Department of the Dallas Medical and Surgical Clinic and Parkland Memorial Hospital, Dallas, Texas

The purpose of this paper is to report a case of a seven-year cure of primary carcinoma of the male urethra with emphasis on the operative procedure employed and the long-term pre- and postoperative period of observation The growth occurred in the bulbous urethra and was removed by an extensive bloc dissection, after which the urethral continuity was re-established by anastomosing the proximal segment of the penile urethra to the membranous urethra by sub cutaneously telescoping the penis backward

The clinical and pathologic features of primary carcinoma of the male urethra have been well summarized by McCrae and Furlong, who made an extensive analysis of all reported cases up to 1950 Of their 239 collected cases, 41 per cent occurred in the "anterior" or penile urethra, 54 per cent occurred in the "posterior" urethra, (bulbous, membranous, or prostatic), with both regions involved in 5 per cent

This lesion is uncommon, and, like cancer elsewhere, its presence may go undetected, while symptoms alone are treated The etiology is uncertain but is perhaps related to chronic irritation associated with an urethral stricture of long standing The most common symptom is obstruction of urination This is often noted in those who are being regularly dilated for a stricture, as an increase in contraction, requiring progressively shorter intervals between dilations Troublesome bleeding, despite gentle instrumentation, also is suggestive

In the review by McCrae and Furlong, the peak incidence was in the 50's with extremes of age being 18 to 91 years Detection of a palpable tumor mass (42 per cent) and fistula formation (32 per cent) were noteworthy features in their series, while recurrent hematuria (10 per cent) as a presenting complaint, was comparatively infrequent

Pathologically, squamous cell carcinoma has been found most frequently in the reported cases and apparently arises by metaplasia from transitional epithelium in the presence of chronic irritation Metastasis to iliac nodes may be expected when the site of origin is in the posterior urethra whereas metastasis to the inguinal nodes is associated with the lesions of the penile urethra In addition, metastases to lung and liver are recorded

Unfortunately in most cases the diagnosis has been made too late to permit curative treatment Without definite treatment no patient was found to have lived over ten months by McCrae and Furlong, who concluded that if the location of the lesion permitted, amputation of all, or part of the penis appeared to give the best results The same authors found that resection of posterior urethral tumors with re-anastomosis or urethrostomy had been successfully carried out

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in 10 of 15 cases, and 5 of the patients so treated were living over 5 years Further discussion of the operative treatment will follow the report of our case

CASE REPORT

Parkland Memorial Hospital No W18792 H A, a 76-year-old colored laborer, was admitted to Parkland Hospital on July 28, 1949, with the chief complaint of a small, hard mass in the perineum, associated with difficulty of urination and hematuria He stated that the mass had been present for one month prior to admission The diagnosis on admission was periurethral abscess

The past history revealed that 11 years previously he had been hospitalized at the same institution for acute retention of urine due to a urethral stricture which subsided after dilations Some difficulty with urination persisted, however, and a few months later a transurethral prostatic resection of a median bar type obstruction was performed The pathologic report of the tissue removed was "fibrous and adenomatous hyperplasia of the prostate" Cystography at that time had shown a small vesical diverticulum

The patient did well thereafter for six years, being seen next in September 1954, when a recurrence of the urethral stricture was noted, and was dilated to 14F with difficulty Periodic dilations over the next four months relieved his symptoms and he failed to return He had had no treatment over the 5 years preceding the current admission

Abnormal physical findings on admission were confined to the perineum where an indurated, nontender, nonfluctuant mass, about the size of a golf ball was palpable A "wooden" consistency was noted by one examiner Rectal examination showed a small fibrous prostate Pertinent laboratory examination revealed mild diabetes and pyuria Attempted cystourethroscopy was unsatisfactory A urethrogram revealed a long stricture of the bulbous urethra with an apparent fistula formation in the area of the mass (fig 1, A) An excretory urogram showed a normal urinary tract and two moderate size diverticula of the bladder

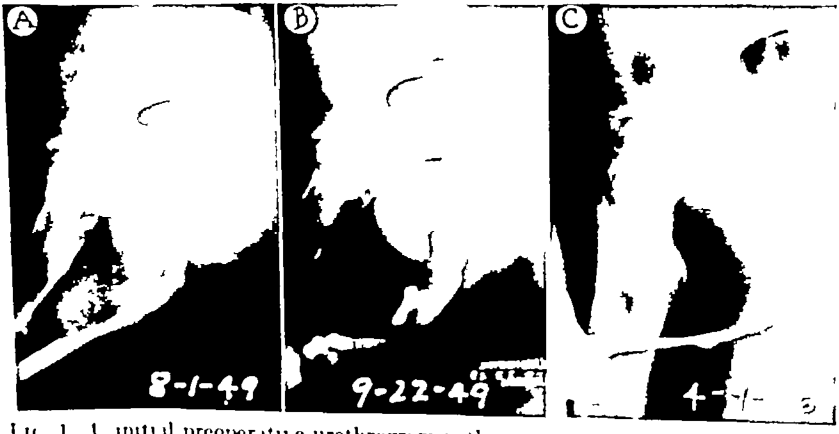

Fig 1 A, initial preoperative urethrogram with apparent extravasation into mass *B*, urethrogram 3 months after excision of carcinoma showing diverticulum and leakage at site of anastomosis Note foreshortening of penis, syringe tip being at external meatus *C*, final urethrogram almost seven years after radical extirpation

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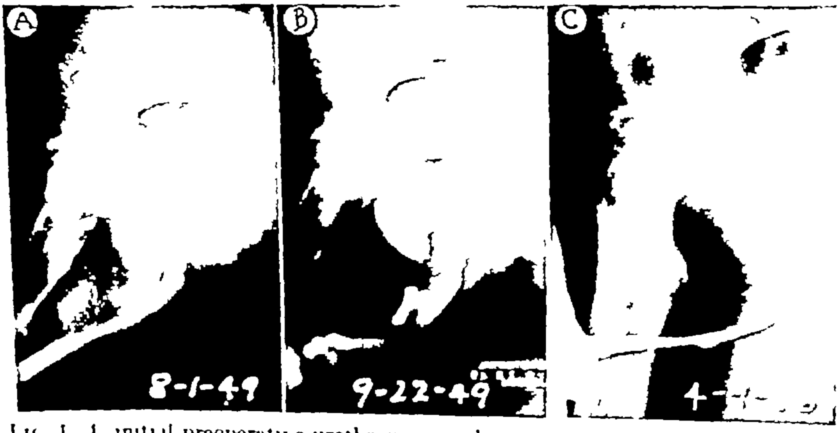


Fig 1 A, initial preoperative urethrogram with apparent extravasation into mass B, urethrogram 3 months after excision of carcinoma showing diverticulum and leakage at site of anastomosis Note foreshortening of penis, syringe tip being at external meatus C, final urethrogram almost seven years after radical extirpation

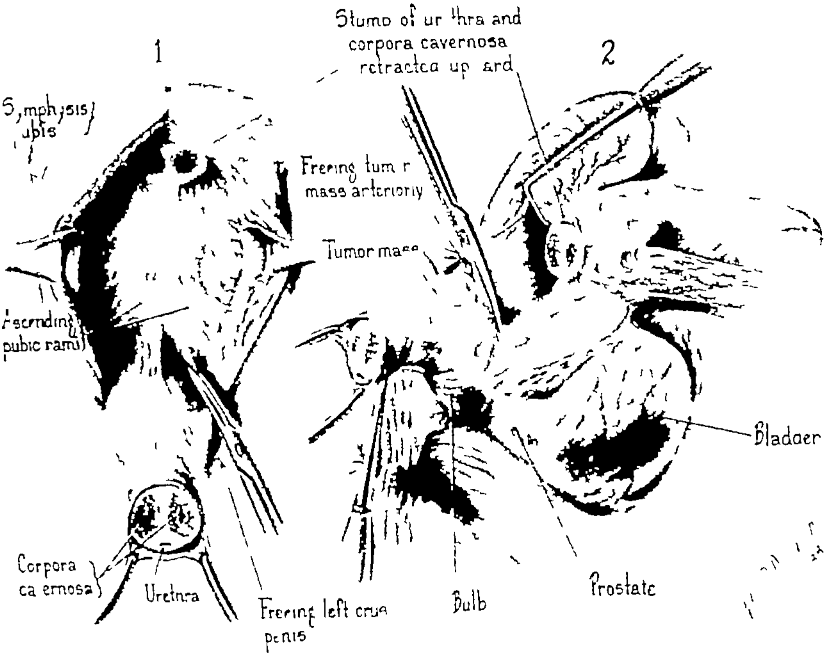


FIG 3 Further operative detail

mation A generous segment was removed for permanent microscopic sections, and the wound closed These sections were reported the next day as "transitional cell carcinoma of medium grade malignancy, with invasion of the perivascular lymphatics Radical removal of the mass was then decided upon with urinary diversion by either permanent perirenal urethrostomy or suprapubic cystostomy, to be determined at the time of operation

Second operation (August 9, 1949) Under spinal anesthesia, with the patient in the exaggerated lithotomy position, a long, midline perineal incision from the midscrotum to a point just anterior to the anus was made Skin flaps were widely undermined on each side The scrotum was retracted forward, and the shaft of the penis freed up subcutaneously, and completely transected 2 cm distal to the mass, which point was at the penoscrotal junction A bloc dissection of the entire mass and adjacent perineal tissues was then carried out from before backward, cutting the crura of the penis at their attachments to the undersurface of the pubic rami on each side (fig 2) The dissection was carried to the triangular ligament and the membranous urethra severed 1 cm proximal to the growth (fig 3) The entire mass, with an incorporated 8 cm section of the urethra, was removed intact (fig 4) The problem of urinary diversion now arose The proximal stump of the membranous urethra was obviously too short to utilize as a perineal urethrostomy It was then found that by a subcutaneous telescoping of the penile shaft backward, the two ends of the severed urethra could be brought into contact without undue tension Accordingly, with a No 22 Foley catheter serving as a

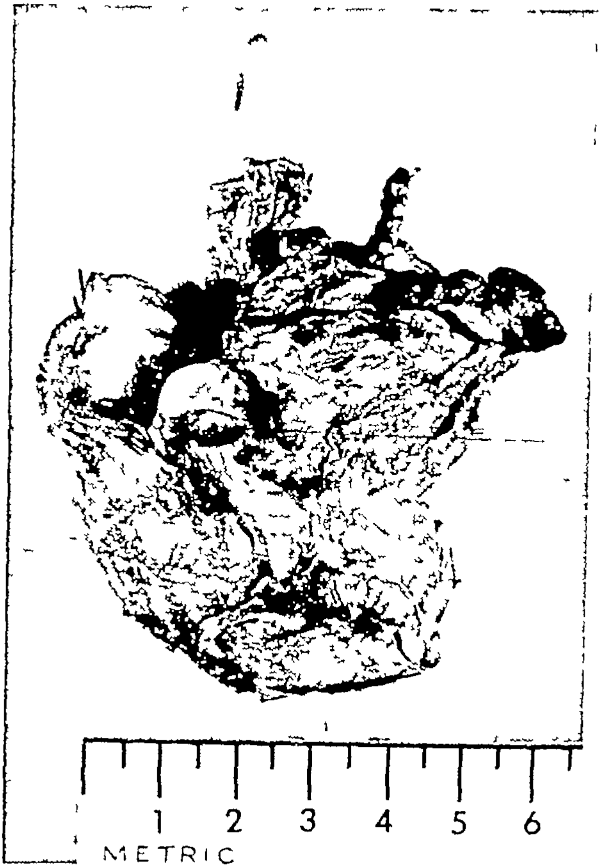


FIG 4 Gross surgical specimen removed in authors' case The segment of urethra removed measured 8 cm

splint, the two ends of the urethra were anastomosed with interrupted 000 chromic sutures, and additional chromic 0 sutures were taken to anchor all three corporal bodies to the triangular ligament (fig 5) The wound was then closed with a small tissue drain emerging posteriorly

Healing was prompt Apparently the dorsal penile vessels were sufficient to sustain the distal penile shaft The splinting catheter was removed on the nineteenth day The patient was discharged on the twenty-third postoperative day, voiding well with good control The penis itself was markedly foreshortened, but otherwise normal

The pathologic report of the removed specimen was transitional cell carcinoma, medium grade malignancy (fig 6)

Approximately three months after the above operation, a small perineal fistula developed and urethrography showed a urethral diverticulum 2 cm distal to the external sphincter, apparently at the site of the anastomosis (fig 1 *B*) This outpouching and fistula were excised, and advantage was taken of the opportunity to biopsy the surrounding tissues No malignant cells were found

The patient did well following this procedure, although dilation of the urethra

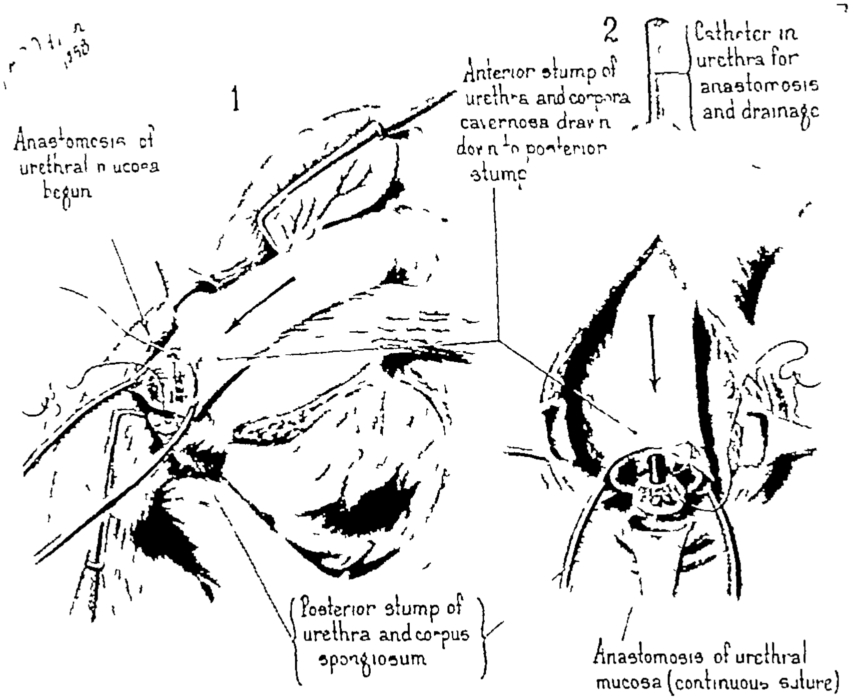

1
2
Anastomosis of urethral mucosa begun
Anterior stump of urethra and corpora cavernosa drawn down to posterior stump
Catheter in urethra for anastomosis and drainage
Posterior stump of urethra and corpus spongiosum
Anastomosis of urethral mucosa (continuous suture)

Fig 5 Penile shaft telescoped backward to permit urethral anastomosis

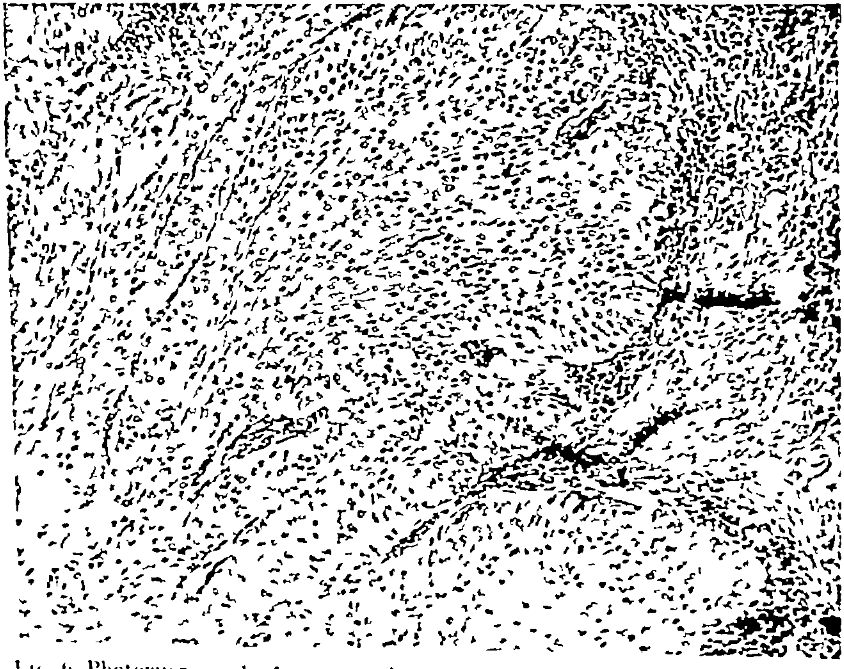
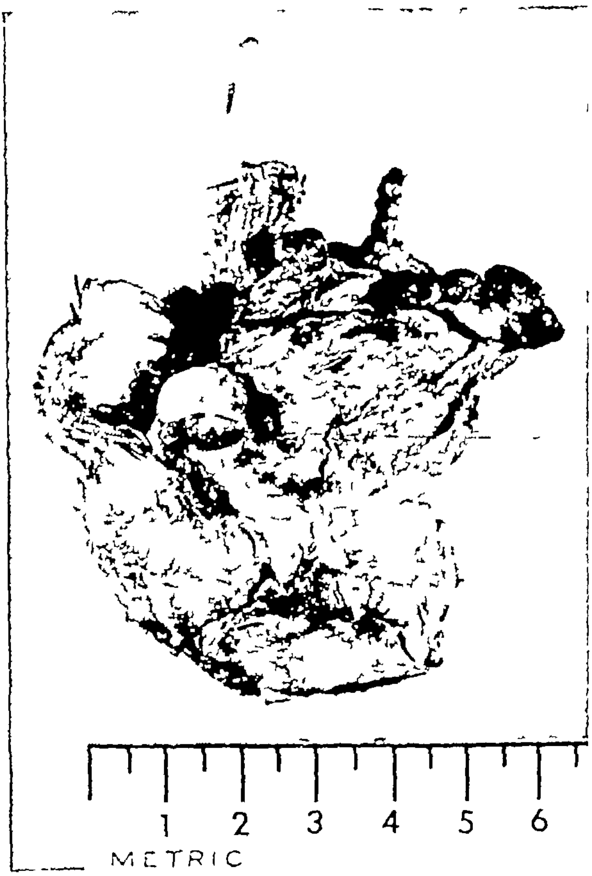


Fig 6 Photomicrograph of specimen diagnosed as transitional cell carcinoma medium grade malignancy



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CARCINOMA OF COWPER'S GLAND

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Cowper's glands receive scant attention and a fatal disorder arising therefrom is a medical curiosity. There had been only eight cases of carcinoma of these organs recorded in the literature until July 1956.[1, 2, 3] Since the accumulation of information could result in an improvement in diagnosis and therapy this ninth case is reported.

CASE REPORT

S. H., New York Hospital No. 701915, was a 51-year-old man who had had a growth" removed through a perineal incision near the urethral bulb three years earlier. After a period of two years his previous difficulty in voiding reappeared. Three transurethral prostatic excisions provided temporary improvements. The tissue removed at the last operation contained an adenocarcinoma and the possibility of origin in Cowper's glands was mentioned by the pathologist. Because a prostatic origin seemed more likely, bilateral intracapsular orchiectomy was performed. An indwelling catheter soon became necessary. When admitted to the New York Hospital on January 23, 1955 a stony hard nodular, fixed mass extended from immediately behind the bulb into the lowermost part of the prostate. Overlying the mass was a well healed 4 cm. surgical scar. The upper third of the prostate was palpably normal. Extension to the right pelvic bones and beside the rectum was evident (fig. 1). The inguinal nodes were not palpable and the remainder of the examination, which included roentgenograms of the bones and chest, provided no indication of metastases. The serum acid and alkaline phosphatases were normal. Endoscopically the prostate appeared adequately resected but irregular white granular tissue lined the urethra from within the prostatic apex to barely within the bulb. An extensive transurethral excision of this tissue permitted voiding but with poor control. Exploration and pelvic node dissection were advised provided the patient was willing to undergo extensive excisional surgery, if the findings suggested that this was feasible. He refused and died 11 months later, approximately four years after his first symptoms. Autopsy was not performed.

The 8 gm. of transurethrally excised chips (Laboratory of Surgical Pathology No. S 55 609) were spongy and softer than the usual fragments of benign prostatic hypertrophy. Occasional minute, glistening translucent nodules protruded from the dull white surfaces. The microscopic appearances were somewhat variegated

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Gresau, W. A. and D. Lipphard: Carcinoma of Cowper's gland. J. Urol., 65: 460-466, 1951.

[3] Kaufmann, E.: Pathology. Philadelphia: P. Blakiston's Son & Co., 1929.

under anesthesia was necessary in March and May 1950, at which time a transurethral biopsy of the operative site was done and no carcinoma found

The patient was well for the subsequent three and a half years, and in fact failed to return to the outpatient department until January 1954 He then had considerable pyuria and a small stream It was believed that two bladder diverticula were the source of the pyuria, and for that reason vesical diverticulectomy was performed, uneventfully

The patient was again seen in May 1956 at which time he returned for routine checkup His only symptom was nocturia two times He was working daily as a yard man Examination showed no evidence of tumor A urethrogram showed a moderate posterior urethral stricture, which was easily dilated to No 20 (fig 1, *C*) The urine contained only an occasional pus cell

DISCUSSION

Apart from the apparent seven-year cure of a case of primary carcinoma of the bulbous urethra, interest in this case centers chiefly upon the operative technique At the time of the removal of the tumor, we were not familiar with the fact that the telescoping procedure had been used after bloc excision in cases of this sort, nor were we aware that such an extensive defect could be bridged by this maneuver We had had some experience with radical excision of stricture in this area with end-to-end anastomosis of the urethra, as described by Maurer, Lich and Burdon However, on reading the literature we found that Dr Hugh Young had performed almost the identical operation a number of years previously, and had reported it under the title "A New Radical Operation for Carcinoma of the Bulbous Urethra A New Use for the Penis", in SURGERY, GYNECOLOGY AND OBSTETRICS, 1939 His operative technique is beautifully illustrated in a series of seven drawings by Mr W P Didusch, three of which are reproduced here

SUMMARY

A seven-year cure of carcinoma of the bulbous urethra, treated by radical surgical extirpation with re-anastomosis of the urethra made possible by telescoping the penis itself backward, is described

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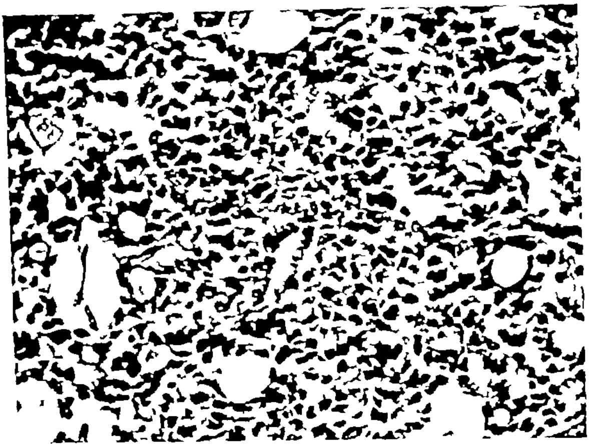


FIG 3 Carcinoma of Cowper's gland Solid areas of pleomorphic cells together with mucus glands H & E × 330

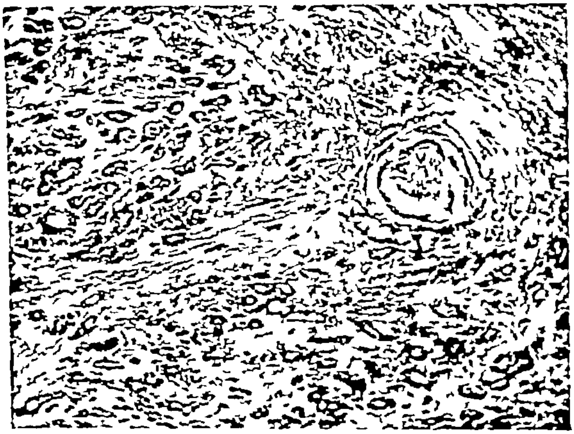


FIG 4 Carcinoma of Cowper's gland Field of scirrhous adenocarcinoma contains nerve sheath invasion H & E × 100

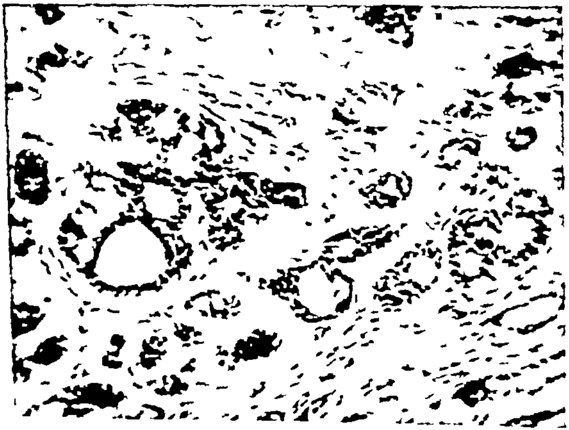


FIG 5 Carcinoma of Cowper's gland Pleomorphic and anaplastic gland forming epithelial tumor cells H & E × 300

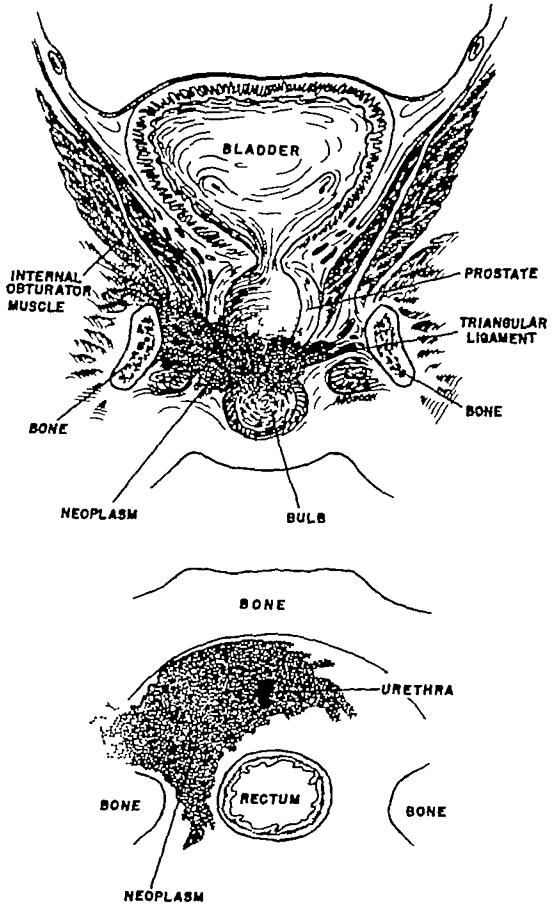


Fig 1 Anatomical location and extent of tumor at time of final transurethral resection
(Upper), showing relation to prostate, etc
(Lower), coronal section through level of external sphincter

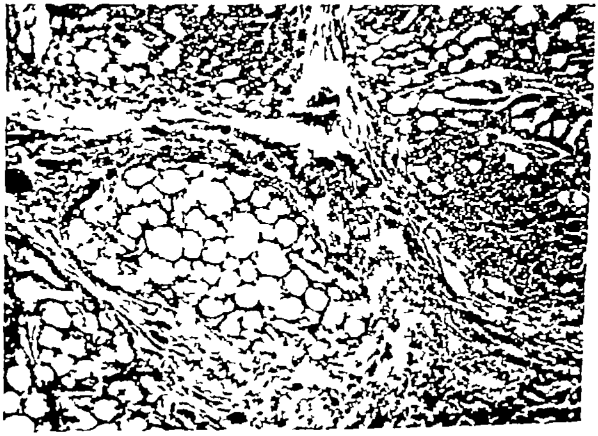
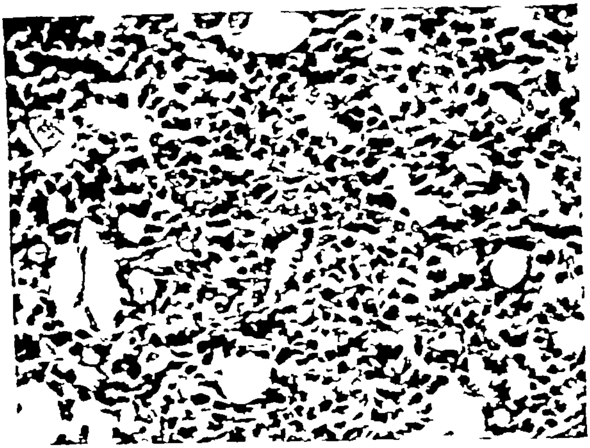


Fig 2 Carcinoma of Cowper's gland Cribriform structures of closely packed mucus-producing glands H & E × 100



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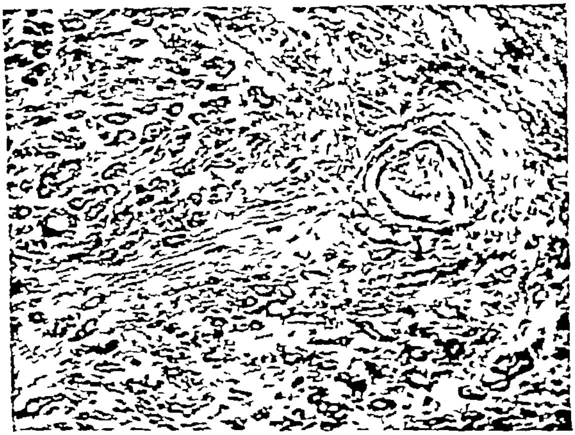

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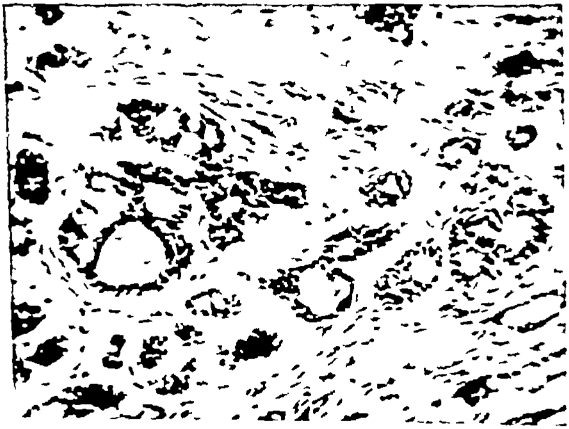

Fig 5 Carcinoma of Cowper's gland Pleomorphic and anaplastic gland forming epithelial tumor cells H & E × 400

but no one fragment differed in its entirety from the others The lesion was obviously a mucus-producing adenocarcinoma with a striking cribriform arrangement in many places Closely packed cuboidal epithelial cells lined the rounded acini and solid intervening areas were filled with similar carcinomatous cells (figs 2 and 3) This pattern was quite unlike that of prostatic carcinoma even in the more scirrhous portions As in prostatic carcinomas there was a marked tendency to invade nerve sheaths or perineural lymphatics (fig 4) Although there was considerable pleomorphism and anaplasia, mitoses were not abundant (fig 5) In the preparations stained with hematoxylin and eosin, the lumina of the glands contained a pale basophilic and often artefactually striated hyaline material that in the *muci-carmine and periodic acid Schiff preparations* gave the reaction for mucin *

DISCUSSION

If the possibility of carcinoma of Cowper's glands comes to mind the diagnosis is not technically difficult The location of the tumor should suggest an origin here Adequate biopsy should confirm this diagnosis because the microscopic appearance is rather characteristic This carcinoma bore a close similarity to several previously recorded The neoplasm was "cylindromatous," while carcinomas of the prostate and urethra are not Urethral cancers in our experience have not contained mucus-producing cells, but have been composed of transitional or squamous cells [4] An origin in paraurethral glands other than those of Cowper cannot be positively excluded

Castration did not produce apparent benefit in this case, nor in the few others recorded Roentgen therapy was not used since the structure of the tumor did not indicate that it would be helpful except in dosages conducive to serious complications A five-year survival has not been reported, although metastases seem to have been *infrequent* These considerations suggest that very radical excision is worthy of trial while the growth is still circumscribable [5]

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* We had thought that the mucinous content of these tumor acini would be strong evidence for their origin in Cowper's mucus producing glands, since the secretions of the normal prostate do not give the histochemical reactions for mucus To substantiate this hypothesis several accepted prostatic carcinomas were similarly stained for mucus To our surprise, although the content of the normal prostatic acini remained unstained, the glands lined by cells that met the cytologic criteria of malignancy were filled with material that was positive for mucus Perhaps this reaction for mucopolysaccharide might be an adjunct in the diagnostic differentiation of carcinoma and benign prostatic adenomatous hyperplasia in those few cases in which structure alone is not the solution

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CONGENITAL TORSION OF PENIS

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Congenital torsion of the penis was first described by Verneuil[1] of Paris in 1857 In 1910, Rocher[2] culled from the literature the 8 cases then recorded and added 11 personal observations In 1922, he[3] added another to bring to 20 the number of reported cases Since then, no additional instance of this lesion has appeared in the literature Treatment of this subject in the English language has been especially limited Only the case of Caddy[4] in 1894, and a brief reference in Campbell's[5] textbook to 5 cases in children can be found Because of the paucity of available material and the curious nature of this rare anomaly, the following case of congenital torsion of the penis and a brief discussion is presented

CASE REPORT

On November 30, 1955 a 20-year-old Negro was examining a pistol when the weapon accidently discharged and the bullet struck him in the right side of the neck He fell and was unable to move his right arm or leg The patient was taken to a local hospital for emergency care and two days later was evacuated to the Neurosurgical Service at Walter Reed Army Hospital

Examination on admission disclosed signs of right hemicord damage at C-7 with ipsilateral hemiplegia and deep sensory loss and contralateral hemianesthesia No further physical abnormality was noted The laboratory examinations were negative A Foley catheter was inserted and paraplegic care instituted

The family history showed this man had 5 sisters and 2 brothers all living and well and without known congenital abnormalities He was married and had three normal children No difficulty had been encountered in achieving and maintaining an erection or carrying out a normal sex act The patient was totally unaware of the unusual state of his external genitalia

On January 20, 1956, a cystoscopy was scheduled The attention of the urologist assigned to the case was immediately drawn to the peculiar formation of the prepuce" Upon closer inspection, it became immediately apparent that this was not the prepuce at all but the frenulum which had come to lie on the dorsum of the penis as the result of an 180 degree torsion of the penile shaft (fig 1) The external meatus was normal A 24 panendoscope was passed into the bladder with ease The course of the urethra, with the scope in place, could be easily palpated along the dorsum of the penile shaft to its base At this point,

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[1] Verneuil Torsion congenitale du penis avec hypospadias Bull Soc de chir de Par, 8 68 70 1857-1858

[2] Rocher H I Torsion congenitale de la verge J de med de Bordeaux 40 737-753, 1910

[3] Rocher H I Torsion congenitale du penis J de med de Bordeaux 94 26 1922

[4] Caddy A A case of congenital torsion of the penis Lancet 2 634 1894

[5] Campbell M Urology Philadelphia W B Saunders Co 1 309 1954

but no one fragment differed in its entirety from the others The lesion was obviously a mucus-producing adenocarcinoma with a striking cribriform arrangement in many places Closely packed cuboidal epithelial cells lined the rounded acini and solid intervening areas were filled with similar carcinomatous cells (figs 2 and 3) This pattern was quite unlike that of prostatic carcinoma even in the more scirrhous portions As in prostatic carcinomas there was a marked tendency to invade nerve sheaths or perineural lymphatics (fig 4) Although there was considerable pleomorphism and anaplasia, mitoses were not abundant (fig 5) In the preparations stained with hematoxylin and eosin, the lumina of the glands contained a pale basophilic and often artefactually striated hyaline material that in the muci-carmine and periodic acid Schiff preparations gave the reaction for mucin *

DISCUSSION

If the possibility of carcinoma of Cowper's glands comes to mind the diagnosis is not technically difficult The location of the tumor should suggest an origin here Adequate biopsy should confirm this diagnosis because the microscopic appearance is rather characteristic This carcinoma bore a close similarity to several previously recorded The neoplasm was "cylindromatous," while carcinomas of the prostate and urethra are not Urethral cancers in our experience have not contained mucus-producing cells, but have been composed of transitional or squamous cells[4] An origin in paraurethral glands other than those of Cowper cannot be positively excluded

Castration did not produce apparent benefit in this case, nor in the few others recorded Roentgen therapy was not used since the structure of the tumor did not indicate that it would be helpful except in dosages conducive to serious complications A five-year survival has not been reported, although metastases seem to have been infrequent These considerations suggest that very radical excision is worthy of trial while the growth is still circumscribable[5]

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* We had thought that the mucinous content of these tumor acini would be strong evidence for their origin in Cowper's mucus producing glands, since the secretions of the normal prostate do not give the histochemical reactions for mucus To substantiate this hypothesis several accepted prostatic carcinomas were similarly stained for mucus To our surprise although the content of the normal prostatic acini remained unstained, the glands lined by cells that met the cytologic criteria of malignancy were filled with material that was positive for mucus Perhaps this reaction for mucopolysaccharide might be an adjunct in the diagnostic differentiation of carcinoma and benign prostatic adenomatous hyperplasia in those few cases in which structure alone is not the solution

[4] Lower W E and Housfeld, K F Primary carcinoma of the male urethra Report of ten cases J Urol 58 192-206 1947

[5] Marshall V F Radical excision of primary carcinoma of the deep male urethra J Urol , 78 252-264 1957

Its occurrence has been ascribed by some to developmental inequality of the corpora cavernosa. In the fully developed organ, the course of the urethra along the torsed shaft can be easily traced by extending a line from the inferior angle of the external meatus to the penoscrotal junction. The urethra itself does not undergo rotation, so that no spiral configuration is developed along its course. In cross-section at any point on the shaft, the urethra is found to maintain its normal relationship with the corpora. Rotation is therefore total, involving all three cavernous bodies to a proportional degree.

The median raphé may assume a variety of configurations. It may be single, double, light or dark, bifid, linear or lozenge-shaped. Generally, the more pronounced the torsion, the lighter and finer the raphé.

Functional impairment is rarely seen with penile torsion *per se*. In Guerlain's[8] case, however, it was necessary for the patient to turn his penis back in order to void. Split or deviated urinary stream, as the result of balanitis hypospadias, is a frequent complaint.

Erection and sexual intercourse usually proceed normally. Procreative ability is modified only by serious degrees of hypospadias or by testicular atrophy which sometimes accompanies this condition.

Operative treatment is most often directed toward the repair of serious degrees of associated hypospadias. Févre, however, has cited the case of Levuef in which a successful reversal of torsion was accomplished by the removal of the crura from the pubis and re-establishing them in normal position.

SUMMARY

The twenty-first instance of congenital penile torsion is reported.

This case is unusual in that first, the rotation is clockwise, second, the rotation is 180 degrees, and third, associated congenital anomalies are absent.

A brief discussion of the clinical aspects of congenital torsion of the penis is presented.

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[8] Guerlain Torsion congenitale de la verge, hypospadias superieur Bull Soc anat de Par 34 87–89 1859

[9] Févre M Treatment of bends and torsions Semaine d hop Paris, 23 895–896, 1947

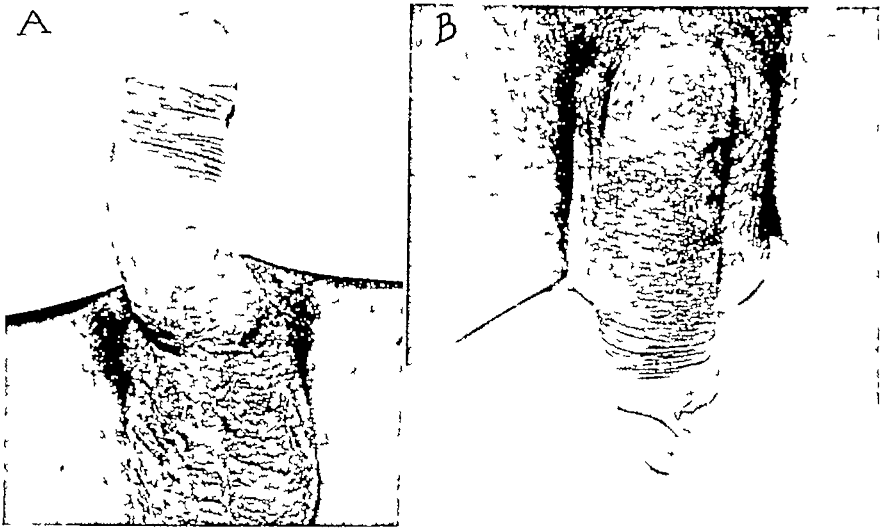

FIG 1 *A*, penis lying over pubis reveals normal dorsal aspect *B*, penis, dependent, discloses frenulum and normal ventral aspect

the urethra then turned deep over the right posterior aspect of the base, thus establishing the rotation as clockwise The endoscopic changes were consistent with those of upper motor neuron lesion and prolonged catheter drainage

The upper urinary tract, investigated by excretory urography, was entirely within normal limits

The patient made satisfactory progress, neurologically, and 3 weeks later was transferred to a veteran's hospital for further care

DISCUSSION

Several aspects of this case are of interest First, the rotation was through a complete 180 degrees, second, the rotation was clockwise, and third, the external meatus was entirely normal, and associated congenital anomalies were absent

Of the 16 cases studied by Rocher,[6] all penile torsions were counterclockwise and the majority were situated at 90 degrees Only one other case of full 180 degree rotation and two other cases of clockwise rotation have been recorded Insofar as can be determined this is the first case of 180 degree clockwise rotation to appear in the literature

Torsion of the penis rarely appears as an isolated congenital anomaly More often it is accompanied by other anomalies, especially of the genitourinary tract Frequently, abnormal development of the ureters or kidneys is seen Almost invariably there is an associated epispadias or hypospadias, especially of the balanitic type Jacobson[7] states that penile torsion uncomplicated by epispadias or hypospadias is almost unknown

The embryologic defect resulting in penile torsion is not clearly understood

[6] Rocher, H L Torsion congénitale de la verge J de med de Bordeaux 40 737-753, 1910

[7] Jacobson W H A Disease of the Male Organs of Generation London J and A Churchill, 1893 p 642

TABLE 1 *Causes of feminization in interstitial cell tumors of adults*

1 The tumors elaborate female hormones
2 The tumors are derived from the Sertoli cells, supposedly the origin of the testicular estrogen
3 The tumors transform androgens into estrogens
4 Extratumoral estrogens are the cause, not the result, of the tumors, as demonstrated in animal experiments [5]
5 The tumors decrease the normal androgen production, resulting in a predominance of estrogens
6 The tumors elaborate abnormal hormones

hyperplasia and neoplasia and to separate interstitial cells from Sertoli cells, granulosa cells, adrenal rest cells, etc Finally, diffuse or localized interstitial cell masses may be associated with other testicular tumors, such as seminomas, embryomas, and teratomas Considering the great variation of the microscopic pictures, one can expect considerable differences in the gross appearance of Leydig cell tumors Some cause an enlargement of the testicle, while others cause a decrease in its size, some involve the organ diffusely, while others form single or multiple nodules or masses Not rarely is the disturbance bilateral Most frequently, however, the diseased organ is enlarged, while that of the opposite side is atrophic In spite of these problems of morphologic interpretation, modern clinical facilities should allow a correct diagnosis in those cases associated with gynecomastia and other symptoms of feminization so that proper treatment can be instituted early before extensive local destruction or distant metastases are encountered In addition, proper preoperative *investigation will enable one to* predict that removal of the neoplasm will reverse the feminization process Such steps were taken in the case to be reported

CASE REPORT

Mr J E K, a 42-year-old refinery worker, was seen on February 21, 1956, because of marked swelling and tenderness of both breasts, a condition which had been gradually increasing during the past four months Previous history was noncontributory, except for a severe penicillin reaction following treatment of an infected tooth with this drug This preceded the onset of the breast swelling by a few weeks However, only sedatives and antihistamines, but no steroid hormones, were prescribed by the family physician at this time Apart from the breast changes, the patient noticed complete loss of libido and a diffuse rheumatic pain along the entire back

Physical examination revealed a normally developed, slightly overweight man in excellent general condition His breasts were symmetrically swollen, soft, and tender, both nipples were enlarged and showed an increase of pigmentation The breasts resembled those of a female in the first trimester of pregnancy However, the patient had otherwise male features, especially male characteristics of skin, hair, muscles, and skeleton Both prostate and testicles were soft and small but the right gonad contained a hazelnut-*sized* hard, nontender nodule, that did not transmit light, sharply demarcated from the rest of the organ The patient was convinced that this nodule had been present for many years and that

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TESTICULAR INTERSTITIAL CELL TUMOR WITH FEMINIZATION IN THE ADULT MALE

H B EISENSTADT AND JAMES L PETRY

An interstitial cell tumor is derived from the interstitial cells of Leydig, first described more than 100 years ago[1] in the normal testicle and situated between the tubular structures Such tumors may occur at almost any age, but are observed most frequently either in childhood or in adulthood during the third and fourth decades of life A considerable number of these growths—but certainly not all of them—exhibit hormonal activity Curiously, their endocrine functions differ greatly in the two above mentioned age groups During childhood, interstitial cell tumors cause precocious masculinization with enlargement of the penis, male hirsutism, deepening of voice, and acceleration of muscular and skeletal development,[1] [3] while in the adult male they produce feminization with gynecomastia, loss of libido, and female hair and skin characteristics [3] [8] The reason for this opposite hormonal function has never been clearly elucidated The precocious puberty of children is explained by an excessive androgen production by the Leydig cells The opposite behavior of the same cell in mature persons has led to the theories[9] [11] listed in table 1

No great strides have been made to prove or disprove any of these suppositions Pathologic studies have not only thrown little light on the existing problems, but they have led to a considerable amount of controversy According to Warren and Olshausen[4] and various other investigators,[12] [13] it is difficult to assess the normal amount of interstitial cell accumulation in various subjects and to distinguish it from primary hyperplasia of unknown etiology, as well as secondary hyperplasia associated with various infections, debilitation, and deficiency diseases On the other hand, it is not always easy to draw the line between simple

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Read at annual meeting of South Central Section of American Urological Association, Mexico City, October 28–November 1, 1957

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[9] Morris, J M The syndrome of testicular feminization in male pseudohermaphrodite Am J Obst & Gynec , 65 1192, 1953

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[13] Christeson, W W and Nettleship, A Interstitial cell growths of the testis Evidence for origin of this cell from seminiferous epithelial cells J Urol , 67 350, 1952

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Table 2

1 Total neutral 17-ketosteroids = 13 5 mg (9–22 mg)
2 17-hydroxycorticosteroids = 7 4 mg (3–10 mg)
3 Corticosteroids (11-oxysteroids, corticoids, cortin) = 14 mg (8–21 mg)
4 Pituitary gonadotrophins (FSH), greater than 6, less than 16 mouse uterine units (6–50 units)
5 Estrogen 60 mg (4–30 mg)

it had not changed in size, form, and consistency The rest of the physical examination was entirely negative

Laboratory results were as follows urinalysis, negative, Kline and Mazzini tests, negative, sedimentation rate, 15 mm per hour (Wintrobe), hemoglobin, 13 7 gm , red cells, 4 2 million, white cells, 6,000 with 44 per cent polynuclears, 49 per cent lymphocytes, 4 per cent monocytes, 1 per cent eosinophils, and 2 basophils Bromosulphalein elimination, cephalin flocculation, thymol turbidity, alkaline phosphatase, prothrombin time, phenolsulfonphthalein excretion, non-protein nitrogen, and blood urea nitrogen were all normal Metabolism was −3 per cent, radio-iodine uptake was 25 6 per cent, cholesterol 230 mg per cent blood sugar—fasting 105 mg per cent, 30, 60, and 120 minutes after 100 gm of glucose orally, 140, 170, and 110 mg per cent X-ray examination of chest and intravenous pyelography were negative, eosinophil count was 250 before and 120 four hours after subcutaneous *injection of adrenocorticotrophin* Urinary hormone determinations per 24 hours are listed in table 2 It is obvious that there was an elevation of estrogens while the other hormones were within normal limits

On the basis of these laboratory and clinical findings, a right orchiectomy and breast biopsy were performed on March 6, 1956 The patient made an uneventful recovery His gynecomastia receded and his libido returned during the next few weeks His 24-hour urinary estrogen excretion on June 24, 1956, was 20 mg per 24 hours

The pathologist, Dr F M Wallace of St Mary's Hospital, Port Arthur Texas gave the following report "*Gross* The testis measured 4 by 6 by 3 cm and contained a firm, movable nodule On section, the nodule was a circumscribed,

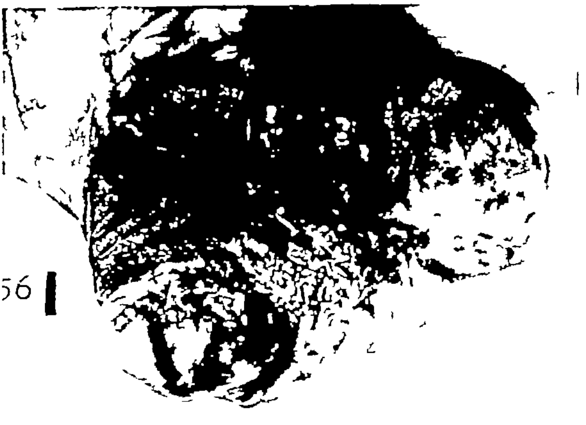

Fig 1

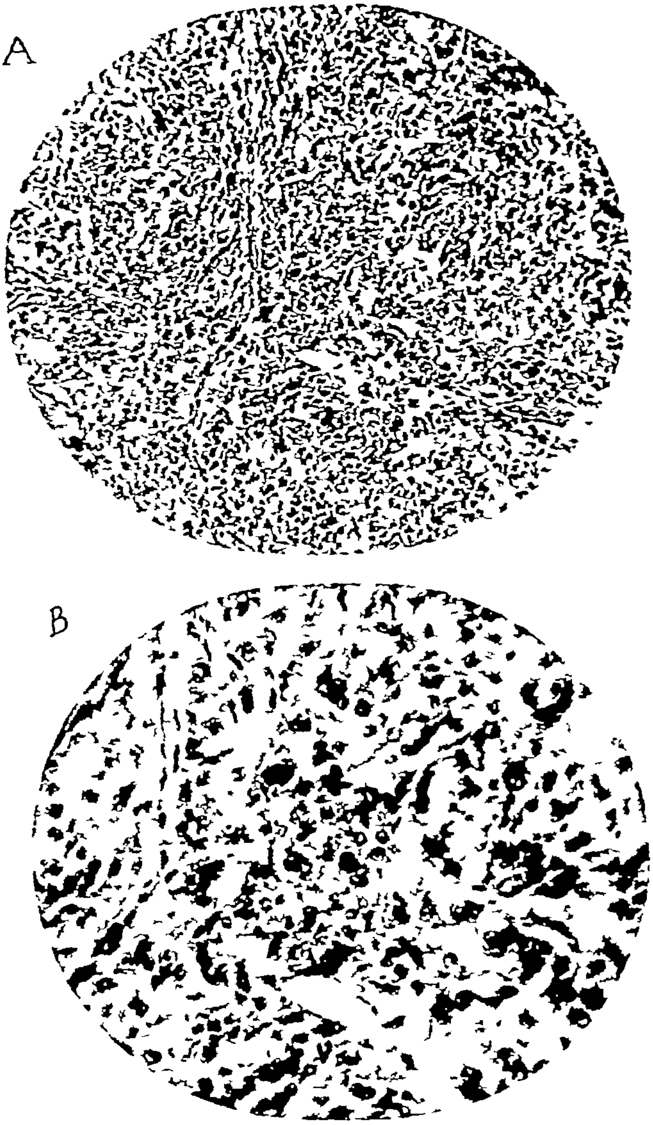

FIG 2

tan, bulging lobulated 1 5 cm tumor There were no areas of hemorrhage or necrosis, and the tumor was distinct from the residual testicular tissue (fig 1)

The breast biopsy measured 1 7 by 1 5 by 0 6 cm and was gray and rubbery

Microsection The tumor was composed of sheets of large cells with little stroma In some areas a fibrous pseudocapsule was present, while in other microscopic fields the tumor compressed hypoplastic seminiferous tubules Glands or glandlike spaces were not present Adrenal cortical and granulosa cells were absent A portion of the center of the tumor was replaced by both loose and

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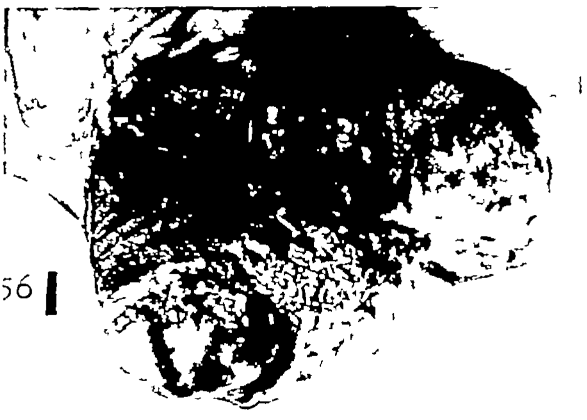
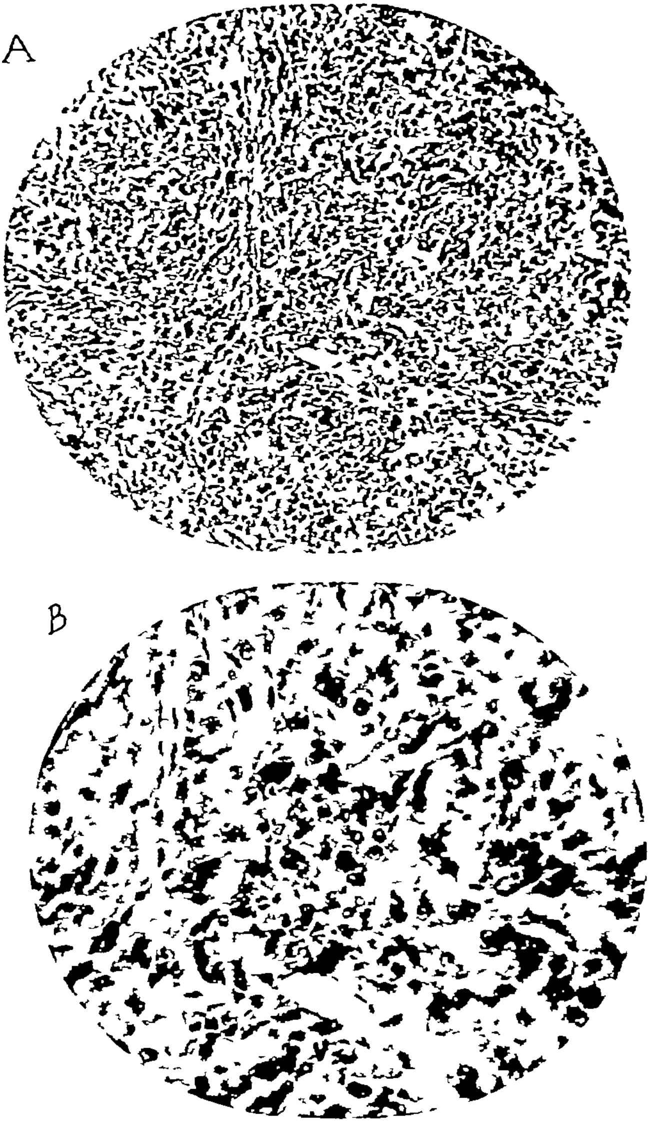


FIG 1



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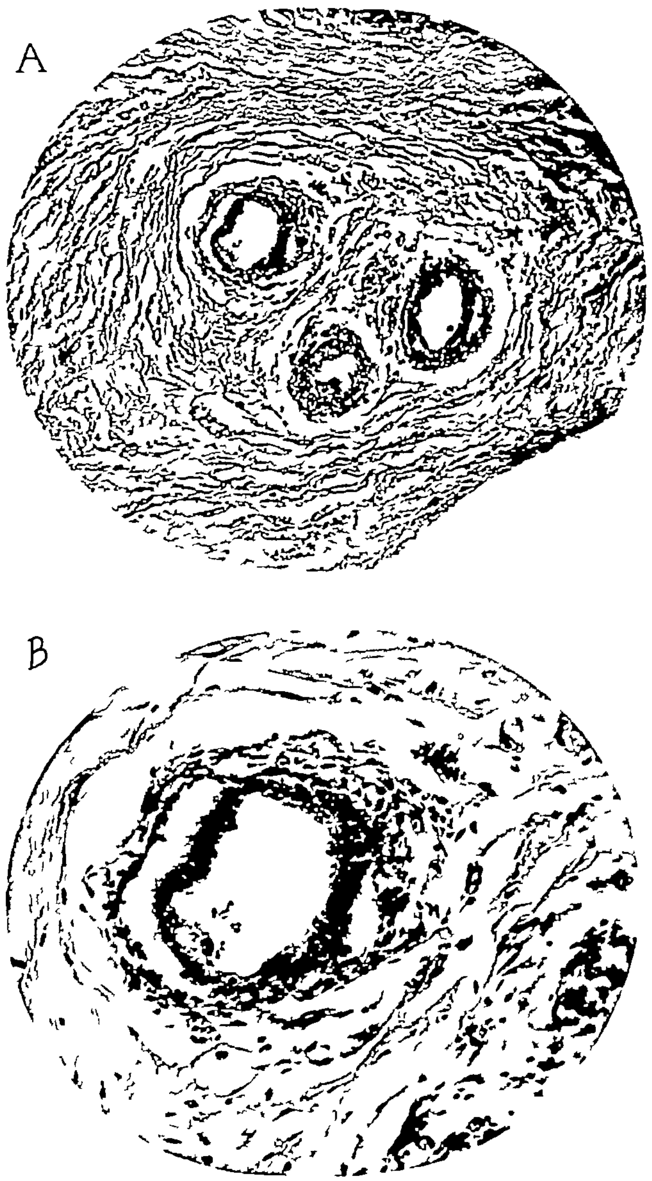

FIG. 3

fibrous hyalin connective tissue. The cell outlines were indistinct and many cells overlapped. The nuclei were round or oval, large, and vesicular, and contained prominent nucleoli. An occasional multinucleated giant cell was present but abnormal forms were not encountered. The cells contained a large amount of acidophilic, granular cytoplasm and no demonstrable pigment, crystalloids, fat, calcium, or inclusion bodies. See figure 2.

"The breast biopsy (fig. 3) contained round and elongated ducts with mature columnar epithelium which was proliferative in some areas. Early attempts at lobule formation were present The stroma was composed of hyalin connective tissue, except for loosely arranged periductal connective tissue Very few inflammatory cells were seen about the ducts"

DISCUSSION

The diagnosis of a feminizing tumor of the right testicle was based, on one hand, upon the clinical findings of gynecomastia, loss of libido, pigmentation of the nipples, testicular and prostatic atrophy, and increased urinary estrogen excretion in the presence of a testicular nodule and, on the other hand, upon the exclusion of the various other causes of such endocrine deviations (listed in table 3)

The long list of abnormal conditions that may enter into the differential diagnosis of a hormonally active interstitial cell tumor is astounding Nevertheless, they all are apparently associated with an imbalance between estrogenic and androgenic substances in the body Normally, both groups of hormones are

TABLE 3 *Differentiation of gynecomastia and other symptoms of feminization*

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1 Pseudogynecomastia of obesity, Fröhlich's and Laurence Moon-Biedl syndromes
2 Transient gynecomastia of infancy, adolescence, senility
3 Cerebral gynecomastia with hypothalamic disturbances, especially tumors, cysts, encephalitis, meningitis, increased intracranial pressure, congenital defects, and dysplasias of the brain
4 Pituitary gynecomastia (hypo- or hyperhormonal) pituitary failure, pituitary eunuchoidism acromegaly, tumors, granulomas, etc
5 Hyperthyroidism
6 Thymic tumors
7 Adrenal gynecomastia (hypo- and hyperhormonal) Addison, adrenogenital syndrome, hyperplasia, or tumors
8 Ovarial gynecomastia precocious puberty, Albright's syndrome, granulosa- and theca cell tumors, teratomas, arrhenoblastoma, chorionepithelioma
9 Testicular gynecomastia (hypo- and hyperhormonal) destruction and disease of the testes by trauma, surgical removal, x-rays and other irradiation, mumps, cryptorchism, Klinefelter syndrome, hermaphroditism, adrenal rest, interstitial cell Sertoli cell, and granulosa cell tumors, embryomas, sarcomas, teratomas, chorionepitheliomas
10 Hepatic diseases cirrhosis, hemochromatosis, hepatitis, hepatoma, etc
11 Pulmonary diseases bronchiectasis, advanced tuberculosis, empyema, primary and metastatic cancer
12 Renal diseases chronic glomerulonephritis and pyelonephritis
13 Spinal cord disease paraplegia transverse myelitis, chordotomy
14 Blood dyscrasias leukemia, malignant lymphomas, mycosis fungoides
15 Chronic infections leprosy, chronic ulcerative colitis
16 Collagen diseases periarteritis, etc
17 Malnutrition, starvation cachexia of malignancies, severe vitamin and protein deficiencies
18 Administration of hormones estrogens, androgens (?), pituitary and chorionic gonadotrophins cortisone, desoxycorticosterone, corticotrophins adrenal extract
19 Administration of drugs digitalis *

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* LeWinn E B Gynecomastia during digitalis therapy New Eng J Med 248 316, 1953

produced by either the testicle and ovary or the adrenal cortices Therefore, any disorder of these organs may be responsible for feminization However, the functions of these glands are influenced by other endocrines as well as by the autonomic nervous system in the hypothalamus, the spinal cord, or the thoracic nerves Furthermore, the sex hormones are partly destroyed in the liver and partly excreted by the kidneys Finally, their production or their disposal may be upset in the presence of deficiency and wasting states or by the exogenous administration of various hormones and related chemical substances (i e , digitalis)

The assumption of such an imbalance of sex hormones as a source of feminization, however, will require confirmation by a widespread use of hormonal analyses It is surprising how rarely such diagnostic steps were taken in the previously reported cases Nevertheless, we can expect that a greater number of interstitial cell tumors will be recognized in the future with the help of careful endocrine investigations Such studies can be further refined when blood hormone levels and fractionation procedures of urinary 17-ketosteroids and of estrogen and progesterone metabolites become available to the practicing physician[8] It may be hoped that then a specific hormone pattern will be evolved characteristic of feminizing interstitial cell tumors that will facilitate not only their early diagnosis, but also their differentiation from other morphologically related neoplasms Finally, repeated hormone analyses could be used to recognize persistence or recurrence of the growth or involvement of the contralateral gonad by the same pathologic process and thus allow a more intelligent approach in the management of these patients

SUMMARY

A small interstitial cell tumor of the testicle was correctly diagnosed, before operation, upon the basis of gynecomastia in a man with a nodule in the right gonad Other causes of feminization could be excluded by careful clinical investigation The value of detailed hormone studies for the confirmation of such a diagnosis is stressed and the need for further refinement of these methods is demonstrated

Too often a patient with gynecomastia or loss of libido is considered to have a functional disorder before all organic causes of such symptomatology are properly eliminated

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MALIGNANT TUMOR OF TESTIS IN INFANT

HARRY Q GAHAGAN AND HENRY C GAHAGAN

This is a report of one patient first seen in 1951 A complete review of the literature has not been made, but no similar case has been seen in the urological journals of recent years A personal communication from Dr Meredith F Campbell stated he had had one patient who was treated by surgery alone

M W , a white boy 19 months of age, was first seen in August 1951 Being a first born, the meticulous mother had noted an increased firmness of the left testis No other signs or symptoms were present His past medical history was negative as was the family history

Physical examination revealed a very well developed and nourished boy who appeared to be in excellent general health The only positive finding was limited to the left testis, which was definitely harder than normal but its size and shape were unchanged No tenderness or fixation was noted and the spermatic cord was uninvolved The right testis and penis were normal Rectal examination was negative

Left orchiectomy was accomplished August 20, 1951 The left inguinal canal was incised initially where the cord was doubly clamped and severed The distal cord and testis were then removed No evidence of direct extension or involvement of nodes was found The patient made a rapid recovery

Section of the left testis showed that all the tissue had been replaced by a light grey homogeneous tumor The microscopic sections revealed "embryonal adenocarcinoma " The diagnosis was made by Dr E C Ulrich and concurred in by Dr J R McDonald

The radiologist advised against postoperative irradiation He did not believe a tumor-killing dose could be given, and he was concerned about the adverse effect on the child's bones

The patient was seen at regular intervals He remained well until August 1956, a total of four years At this time he rapidly lost weight and looked pale A retroperitoneal mass developed in the left upper quadrant Urinalysis, excretory urogram, series of gastrointestinal films and chest x-ray were negative

Exploration of the left retroperitoneal area revealed such extensive involvement of the retroperitoneal nodes that node dissection was considered impossible, therefore, a large biopsy was the only accomplishment

Microscopic sections this time showed very anaplastic tissue (fig 1) Dr Lewis B Woolner simply classified this as "clear cell carcinoma, grade four "

A few x-ray treatments were given but were discontinued by the parents However the patient lived until November 1956, fifteen months after biopsy, and died from generalized carcinomatosis

SUMMARY

A 19-month-old boy was seen because of a hard left testis An orchiectomy was done immediately and the testis was found to be replaced by tumor, the diagnosis was embryonal adenocarcinoma No postoperative x-ray therapy was given

Accepted for publication March 18 1957

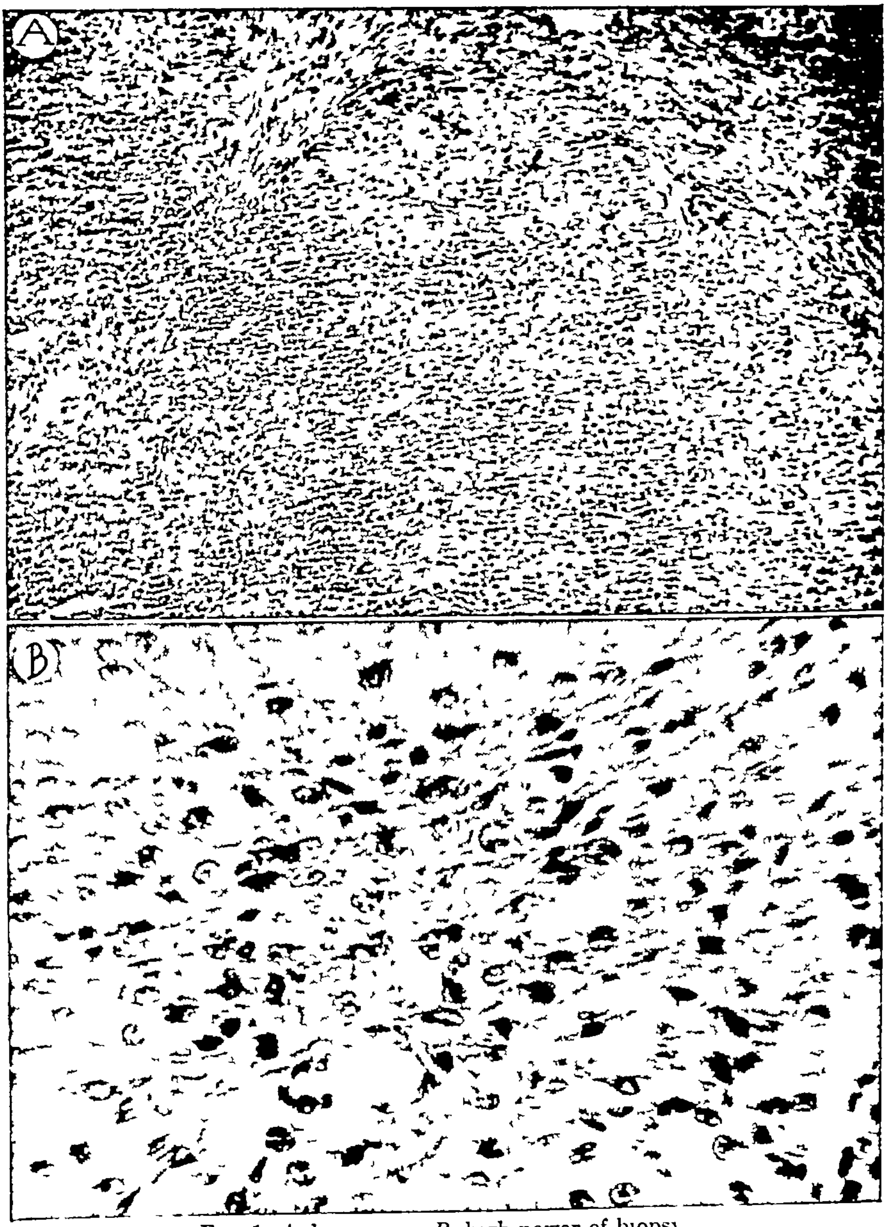

FIG 1 *A*, low power *B*, high power of biopsy

Extensive left retroperitoneal metastasis occurred 4 years later A biopsy at that time was reported as "clear cell carcinoma, grade four" The patient expired 15 months later from generalized carcinomatosis

Addendum Soon after submitting this case report a teratoma of the testis in a sixteen-month-old infant was reported by Meyer and Coughlin (J Urol, 77 285, 1957) Subsequent retroperitoneal node dissection was done and no positive nodes were found The child was living and well three years later

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EFFECT OF DIVISION OF THE TESTICULAR ARTERY ON VIABILITY OF THE TESTIS IN MAN

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The testicular artery was advantageously divided during the three following operations 1) In a pyeloplasty which lent itself to the method described previously (Maluf, '56), the testicular artery, arising from a lower polar renal artery, was severed so as to mobilize adequately the polar artery for closure of the defect through which the renal pelvis and upper ureter bulged 2) During an orchiopexy, in order to deliver an intra-abdominal testis into the scrotum, the relatively short testicular vessels were divided with reliance on the carefully guarded vasal artery and vein for blood supply to the testis 3) In the performance of nephrectomy for renal adenocarcinoma we habitually stay outside of Gerota's fascia, removing all enclosed structures, including the testicular vessels, down to the pelvic brim 4) In a transperitoneal retroperitoneal lymphadenectomy for unilateral embryonal cell carcinoma of the testis the contralateral testicular artery was excised when it was in the way of removal of juxta-aortic nodes, lymphatics, and other tissue (fig 1) During execution of the above lymphadenectomy opinions conflicted as to whether the human testis atrophies after division of its artery Harrison ('49) noted that ' There is no unanimity in the literature concerning the effects of division of the testicular vessels in Man " Nothing has appeared since then to satisfy the query so far as we know Our purpose was to make controlled observations of the human testis before and after division of its artery

METHOD

Three male patients with untreated prostatic adenocarcinoma metastatic to bone volunteered for bilateral orchiectomy in two stages Diagnosis was confirmed by perineal punch biopsy of the prostate under local infiltration with 1 per cent xylocaine HCl The patients did not have pain or ureteral obstruction and thus were not in immediate need of hormonal therapy Their initial 24-hour urinary excretion of 17-ketosteroid† was measured This was followed by the "first stage" of orchiectomy Both testes and spermatic cords were exposed under regional block with 1 per cent xylocaine HCl, a biopsy was taken from each testis, then the testicular artery and the anterior cluster of veins of the pampiniform plexus were divided Division of the artery was confirmed in cross-section A few weeks later the patient was readmitted and his urinary excretion of 17-ketosteroid in 24 hours was measured again The second stage consisted of bilateral orchiectomy All specimens were examined by the patholo-

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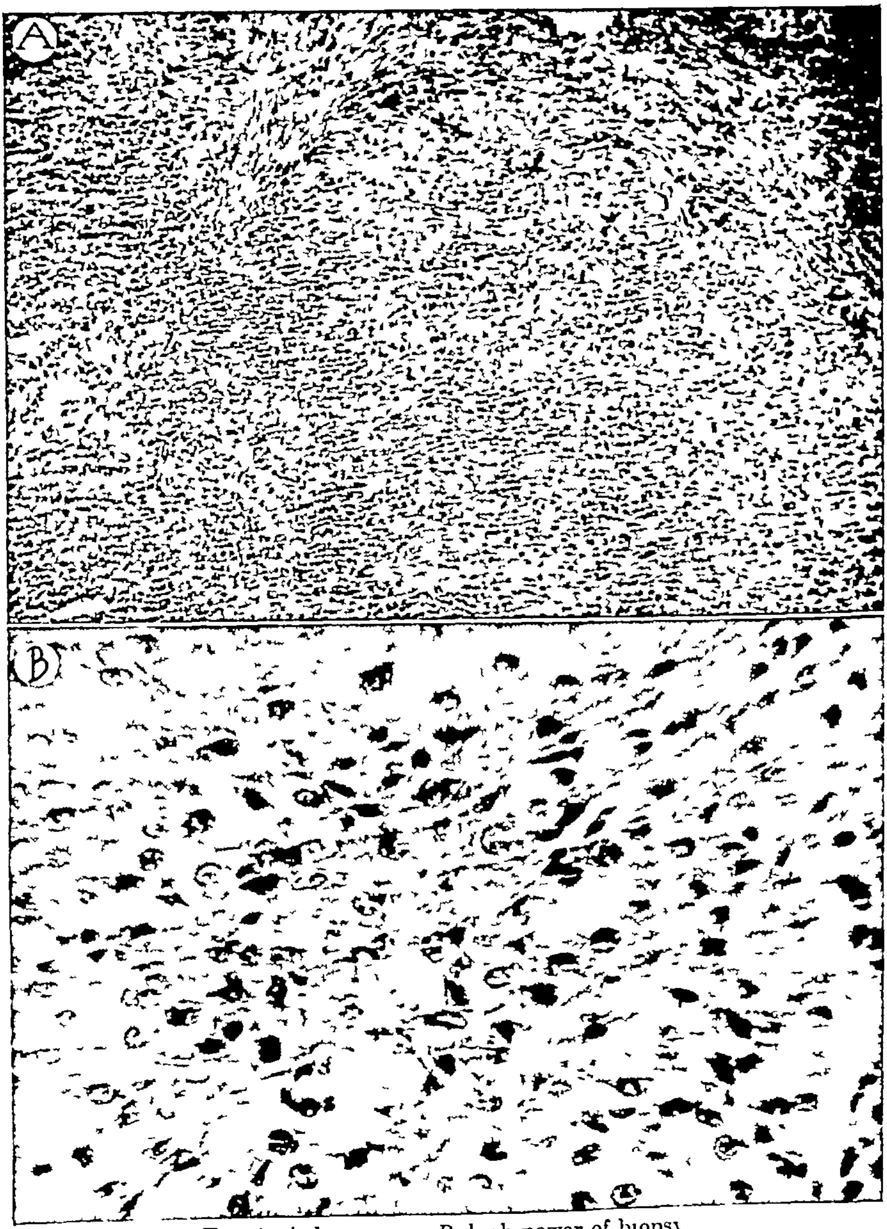

FIG 1 *A*, low power *B*, high power of biopsy

Extensive left retroperitoneal metastasis occurred 4 years later A biopsy at that time was reported as "clear cell carcinoma, grade four" The patient expired 15 months later from generalized carcinomatosis

Addendum Soon after submitting this case report a teratoma of the testis in a sixteen-month-old infant was reported by Meyer and Coughlin (J Urol, 77 285, 1957) Subsequent retroperitoneal node dissection was done and no positive nodes were found The child was living and well three years later portion of each preserved for microscopic study Microscopic The seminiferous tubules are lined by cells three to five nuclei deep In one testis, some are partially or completely hyalinized Spermia are present Leydig cells are conspicuous and in groups At one margin, around the epididymis, there is granulation tissue infiltrated with lymphocytes, plasma cells, and large mononuclear cells, many contain golden brown granules and focal areas of multinucleated giant cells of the foreign type Around the tubules of the epididymis are infiltrations of lymphocytes and plasma cells In the opposite testis, the inflammatory reaction is not conspicuous "

Case 2 (VAH 54401) was a 59-year-old Caucasian male with adenocarcinoma of prostate, acute urinary retention, and generalized metastases to bone On April 29, 1955 a urethral catheter was left indwelling The blood urea-N, hemoglobin, hematocrit, and serum acid and alkaline phosphatase levels were normal On May 2 his 24-hour urinary excretion of 17-ketosteroid was 9 3 mg On May 4 bilateral testicular biopsy and division of each testicular artery were done The pathologist's report of the biopsies was identical microscopically with that of the entire testis (below) The patient was discharged with indwelling balloon catheter On June 8 and 9, 24-hour urinary excretion of 17-ketosteroid was 4 7 and 6 2 mg, respectively On June 10, intravenous pyelography showed poor concentration by the right kidney On June 13 a suprapubic vesicocapsular partial prostatectomy and bilateral orchiectomy were performed Pathological report of the testes stated, 'Seminiferous tubules lined by cells 2 to 3 nuclei deep, spermia present, nests of Leydig cells present Cells lining tubules of the epididymis are preserved, occasional spermia noted in lumina "

Case 3 (VAH 56213) was a 63-year-old Caucasian male with adenocarcinoma of prostate metastatic to the skeleton The intravenous pyelogram, blood urea nitrogen, serum creatinine, and serum acid phosphatase were normal On June 9 his 24-hour urinary excretion of 17-ketosteroid was 5 22 mg and on June 10 it was 4 64 mg (total 24-hour urinary volume, 5,380 cc) On June 17 he underwent bilateral testicular biopsy and division of each testicular artery together with division of the anterior cluster of veins of the pampiniform plexus Biopsy report stated that the seminiferous tubules are lined by cells two to three nuclei deep These cells are large and vacuolated Spermia are absent There is slight increase in interstitial fibrous tissue " On July 20 it was noted that his testis showed no clinical change in size or consistency On July 20 his 24-hour urinary excretion of 17-ketosteroid was 5 2 mg (total volume of urine 2 060 cc) On July 25 he underwent bilateral orchiectomy The pathologist's report was thus "Gross Specimen A consists of the right testis and epididymis, 6 by 4 by 2 5 cm Cut surfaces are similar to A Microscopic A) The seminiferous tubules are lined by one to three rows of cell nuclei Around these is an increased amount of hyalinized connective tissue Spermia are absent In the intertubular loose connective tissue there are groups of Leydig cells B) It is essentially similar to A "

Case 4 (KFH* 569168) was a 56-year-old Caucasian male who underwent

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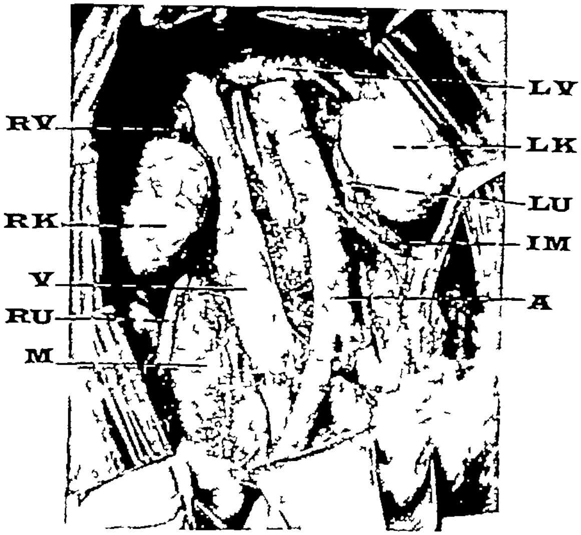

FIG 1 Photograph of retroperitoneum of 25 year old man (VAH 43816) immediately after completion of transperitoneal retroperitoneal lymphadenectomy for embryonal cell carcinoma of right testis This procedure performed by Dr Oscar Creech, Jr , and the writer, will be published in detail later Note absence of *both* testicular arteries, removed in the operation A, aorta, *IM*, inferior mesenteric artery , *LK*, left kidney , *LU*, left ureter, *LV*, left renal vein, *M* right psoas muscle, *RK*, right kidney , *RU* , right ureter, *RV* right renal vein, V inferior vena cava

gists Béla Halpert, M D , Ethel E Erickson, M D (cases 1 and 3) and Rodney Carleton, M D (case 4)

RESULTS

The findings will be described according to case

Case 1 (VAH 54653) was a 61-year-old Caucasian male with adenocarcinoma of prostate metastatic to bone His serum acid phosphatase was elevated On May 2, 1955 his 24-hour urinary excretion of 17-ketosteroid was 4 8 mg On May 3 he underwent bilateral testicular biopsy and division of each testicular artery Tissue examination was as follows "Gross Specimen A consists of a portion of brown tissue 0 6 by 0 5 by 0 4 cm Cut surfaces are similar Specimen B consists of a similar portion of tissue 0 4 by 0 3 by 0 2 cm All preserved for microscopic study Microscopic A) The seminiferous tubules of the right testis are lined by cells five to six nuclei deep, in these adult spermia are noted Others are completely hyalinized Varying sized groups of Leydig cells, some rather large, are conspicuous " On the third postoperative day the testes were noted to be somewhat tender but not enlarged On June 3 and 6 the 24-hour urinary excretion of 17-ketosteroid was 5 53 mg and 8 73 mg , respectively On June 7 bilateral orchiectomy was performed Tissue examination was as follows "Gross Specimen consists of 2 testes and epididymides One is 6 by 4 by 2 5 cm and the other is 6 by 4 by 3 cm The surface is smooth and glistening The cut surfaces are beige and the tubules tease with ease The epididymis is gray The surfaces of the second testis are raw with gray-white tissue On cut surface an area of hemorrhage in the center is noted 1 cm in diameter Representative abdominal testis at the internal inguinal ring This testis was small (2 by 1 by 1 cm) and orchiectomy was elected The hernial sac was resected, the peritoneum closed, and the spermatic cord was mobilized and divided with care against injuring the vas deferens and its vessels The testis was freed entirely except at its attachment to the vas deferens Nevertheless there was a steady flow of bright red blood from the cut margin of the tunica albuginea which ceased instantly after clamping the vas deferens and its vessels

Other cases In the performance of nephrectomy for renal adenocarcinoma we habitually stay outside of Gerota's fascia and remove all enclosed structures down to the pelvic brim In so doing the ipsilateral testicular vessels are sacrificed We do not actually see the kidney during the operation In our six cases the diagnosis of adenocarcinoma was established by the pooling of the injected contrast medium during aortography *There has been no clinical change in the corresponding testis after such a radical nephrectomy* In one such patient the ipsilateral, left varicocele regressed completely (figs 70 to 73 in Maluf and McCoy, '55), much to the patient's satisfaction

DISCUSSION

1 *Effect of division of the testicular artery in animals* Ligation or division of the testicular artery results in atrophy of the testis in dogs (Cooper, 1830, Miflet, 1879, Griffiths, 1896, Moschcowitz, '10, Wangensteen, '27, Joranson et al, '29), guinea pigs and rabbits (Schinz and Slotopolsky, '24, Wangensteen, '27), and rats (Oettlé and Harrison, '52) Ljubomudrow ('30) found testicular atrophy in two out of five dogs after ligation of the testicular artery The other three dogs showed anastomoses between the vasal, cremasteric (external spermatic), and external pudendal arteries By injecting gelatin into the testicular artery of dogs, Capurro ('01/'02) showed that at least capillary communications exist between the testicular artery and the vasal and cremasteric arteries Harrison ('49) could not detect any such connections greater than capillary size in dogs He noted that vascularization of the testis in dog and rat differs from that in Man by absence of direct anastomosis of the testicular artery with the vasal and cremasteric arteries "Unconditional application of the results of division of the testicular vessels in experimental animals to Man is therefore not valid"

2 *Effect of division of the testicular artery in man* The testicular (internal spermatic) artery of Man has multiple arterial anastomoses with the vasal artery at the level of the epididymis In this region, too, there are arterial anastomoses between the testicular artery and the cremasteric (external spermatic or funicular) artery (Sappey, 1873, Jarisch, 1889, Colle, '02, Picqué and Worms, '09, Hill, '09, Golder, '40, Harrison and Barclay, '48, Harrison, '49, Barclay, '51, Testut and Latarjet, '49) Haberer (1898) presented a thorough study, done while a medical student, of the venous drainage from the testis Harrison ('49) observed that in fifty separate mammalian species, in which the testicular artery was injected with "chlorbismol" consisting of particles too large to pass through capillaries (10 μ to 12 μ), the only two species other than Man in which the cremasteric artery was filled by retrograde injection were the chimpanzee and

radical cystectomy, bilateral ureterosigmoidostomy, and sigmoid colostomy through a Cherney† incision on August 25, 1956 for infiltrating carcinoma of the bladder During this procedure the abdominal portion of both spermatic cords and the intrapelvic portion of the vasa deferentia with accompanying vessels were removed Each deep epigastric artery was divided cephalad of the origin of the cremasteric artery The testes thus had the following maximal arterial supply cremasteric, superficial pudendal, and deep pudendal (fig 2) Both testes swelled moderately but gradually regressed to stable size The right testis was the size of a large hen's egg and the left that of a small hen's egg Bilateral testicular biopsy was performed three and a half months later under regional block The right testis disclosed well-formed seminiferous tubules lined by Sertoli cells exclusively Interstitial cells were present The left testis disclosed fibrous tissue which was interpreted as secondary to infarct of testis

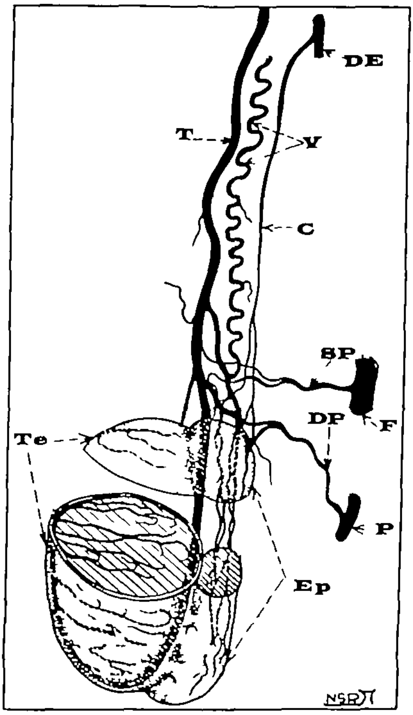

FIG 2 Semi-diagram of lateral aspect of left testis and epididymis demonstrating arterial supply to both structures *C*, cremasteric (external spermatic, funicular) artery, *DE*, deep epigastric artery, *DP*, deep pudendal artery, *Ep*, epididymis, *F*, femoral artery, *P*, pudendal artery, *SP*, superficial pudendal artery, *T*, testicular (internal spermatic) artery, *Te*, testis, *V*, vasal artery (Adapted from Jarisch, 1889 Ljubomudrow, '49, Barclay, '51, and especially Harrison and Barclay '48, and Harrison '49) *It is doubtful whether any collaterals other than those from vasal artery can support spermatogenesis Even vasal artery, in certain percentage of cases, may be inadequate after occlusion of testicular artery*

Case 5 (KFH 588682) was a 23-year-old man with left undescended intravessels are not divided This is probably due to accidental tearing of some of the trunks In this connection it is of interest that Harrison ('49) suggested that the anastomoses between testes and vasal arteries are poorer in young persons 'This was demonstrated by injection of the testicular artery with chlorbismol in the testes of two boys aged 8 and 10 years In the former only the vasal artery was filled by retrograde injection through two small anastomotic channels on the body of the epididymis In the latter neither the vasal nor the cremasteric arteries was filled It can therefore be conceded that any damage to the testicular vessels during orchiopexy may lead to atrophic changes in the majority of cases Staemmler ('23) found the testicular arteries of undescended testes in men of 20 to 30 years of age to have a markedly narrowed lumen with thickening of the intima

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† Cherney, L S A modified transverse incision for low abdominal operations Surg, Gynec & Obst, 72 92–95, 1941

Burdick and Higinbotham ('35) divided the entire spermatic cord during inguinal herniorrhaphy in 200 cases They noted that 'many of the testicles atrophy in fact, some almost completely disappear but it is surprising how many do not The testis was recorded as normal in size in 42 out of the 169 cases followed A fairly common observation was moderate swelling of the testicle for one or two months after operation followed by diminution in the swelling to normal or going on to atrophy" No histological studies were reported Residual blood supply could be only through cremasteric and pudendal arteries (fig 2) as in our case 4 It appears that the moderate postoperative swelling was due to infarction and that this was followed by fibrosis, as in the left testis of our case 4 Neuhof and Mencher ('40) divided the spermatic cord between the external and internal inguinal rings in 24 selected cases of inguinal herniorrhaphy The testes remained normal to clinical inspection in less than 68 per cent and underwent obvious atrophy in 32 per cent "Microscopic study of the testis removed in one of these cases thirty-one months after complete severance of the structures of the cord revealed an essentially normal testis'

SUMMARY

The testicular artery was divided bilaterally in three elderly patient-volunteers as the first stage' of orchiectomy for metastatic adenocarcinoma of prostate Histological appearance of the testis and 24-hour urinary output of 17-ketosteroid showed no essential change after division of the testicular artery

Division of the spermatic cord proximal to the external inguinal ring and of the vas deferens and its vessels in one middle-aged patient resulted in abolition of spermatogenesis in one testis and in infarction of the other testis followed by fibrosis

Division of the testicular artery to an atrophic undescended testis in a 23-year-old man did not obliterate the entire arterial supply to that testis

It is concluded that it would be permissible to divide the testicular artery in the abdomen if a surgical advantage would be gained Testicular atrophy from such a procedure would be unlikely

The pertinent literature is summarized

gibbon He furthermore noted that in about one-third of human cases there is no important anastomosis between the testicular and cremasteric arteries In one-third of the cases arteriography indicated that the sum of the diameters of the cremasteric and vasal arteries was equal to, at least, the diameter of the testicular artery In our case 4 the testes could have received blood only through the cremasteric and pudendal arteries That this was inadequate was shown by infarction of the left testis and survival of only interstitial and Sertoli cells of the right testis In the rat testis, at least, these cells have been shown to be least sensitive to ischemia (Oettlé and Harrison, '52)

What happens to a human testis after its testicular artery has been severed has not been established Various clinical observations indicate that the testis may survive even after the testicular artery has been divided or totally obstructed This evidence falls under three categories *a Division of the pampiniform plexus for varicocele* In the bad ' old'' operation for varicocele in which the pampiniform plexus was excised, the testicular artery, which typically courses through this plexus, was often inadvertently severed Clinically at least, the testis remained essentially normal (Sappey, 1873, Kocher, 1887) Bevan ('04) reported that, in over 100 operations for varicocele, all structures of the cord except the vas deferens and its vessels were severed without producing evidence of "nutritive deficiency" of the testis No microscopical studies or biopsies were reported *b Obliteration by aneurysm* Sappey (1873) found a viable testis in a case in which an aneurysm had obliterated the testicular artery at its origin Wardrop, on the other hand, observed that bilateral testicular atrophy occurred in a middle-aged man during progress of an aortic aneurysm in which the orifices of the testicular arteries became blocked (cf Griffiths, 1896) *c Division of the testicular vessels during orchiopexy and herniorrhaphy* Mignon ('02) stated that all vessels of the spermatic cord, except those accompanying the vas deferens, could be sacrificed without producing outward change of the testis He thus advocated performance of orchiopexy for undescended testis by dividing the testicular vessels Bevan ('04) noted that in most cases it was possible to bring the undescended testis into the scrotum by merely mobilizing the testicular vessels In the few in which this was not possible the testicular vessels were divided He then never failed to bring down into the scrotum an intra-abdominal testis Absence of external change of the testis was explained by blood supply from the vasal artery No microscopical studies were done Moschcowitz ('10) stated that ' If further proof were wanting, the results of the Bevan operation speak for themselves In no case of my series did necrosis of the testicle occur, and the preservation of erectile power is to a certain extent, proven by the maintenance of perfect potentia coeundi in one adult case of bilateral undescended testes which I operated '' He advised handling the vas deferens with care to avoid damaging its artery No histological studies were mentioned Mixter ('24) reported his results with 168 orchiopexies There were 15 cases with intra-abdominal testes, all of which underwent division of the testicular artery and vein for adequate mobilization Thirteen of these underwent gross testicular atrophy He noted, however that atrophy may ensue where the spermatic

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CLINICAL VALUE OF EPIDIDYMO-VESICULOGRAPHY

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The first seminal vesiculography was performed by Belfield[1] in March 1913 when he used a 5 per cent solution of collargol as an opaque medium and injected the solution into the vesicles through a vasotomy opening Also in the same year, Young, Waters and Luys applied the same diagnostic procedure in their own clinical patients From then on, the subject of x-ray investigation of the seminal vesicles has been the title of several papers which were published in this country as well as overseas However, in 1951, Braasch and Emmett[2] reviewed the previous works on this subject and brought the data up to date in their book, CLINICAL UROGRAPHY Also, in March 1953, Pereira[3] published his comprehensive paper concerning a detailed and accurate review of the history, methods, clinical use and his own interpretation of seminal vesiculography Pereira's paper is the most interesting and informative piece of work available on this subject

As far as epididymography is concerned, one may say it did not appeal to the urologists until May 1952 when Boreau, Hermann, and Vasselle[4] published their first paper on this subject Following this presentation, other European authors such as Korkud,[5] 1952, Perruzzo and Antonini,[6] 1953, as well as Trabucco and Bottini,[7] 1954, also participated in studying epididymography and its use The most complete study on this subject is that of Boreau and all[8, 9] in 1953

In summary, the review of the literature reveals that the x-ray examination of the seminal tract and interpretation of it still are in the embryonic stage Whatever had been said in this field did not extend beyond the limits of interpretation of chronic seminal vesiculitis until November 1954 when Abeshouse, Heller and Salik[10] published the paper concerning some other disorders of the seminal tract such as tumors of the testis, tuberculosis of epididymis and obstruction of the vas deferens Following this presentation, Comarr and Bors[11] (1955) published a

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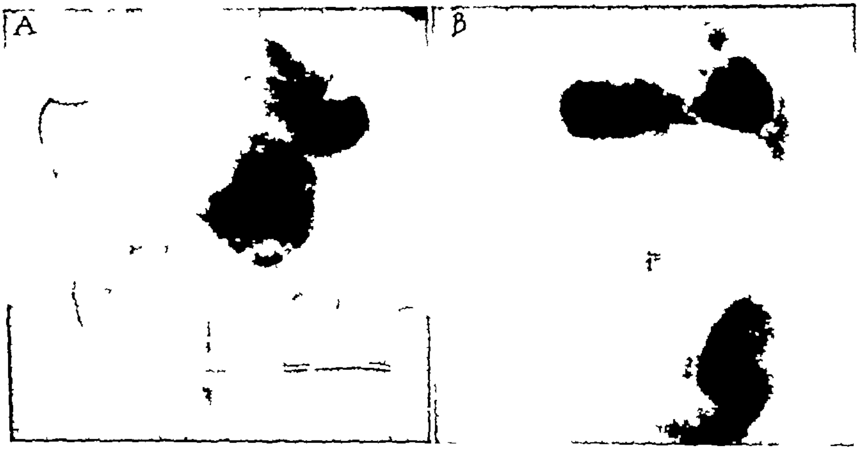

FIG 2 Case 2 H W , 20, No 15152 Clinical diagnosis Uveitis and normal genito-urinary tract X-ray diagnosis Normal seminal vesicles A, immediately after injection of opaque medium B, 10 minutes later

*a Seminal vesicles represent the confluence of a few or several small round or elongated saccules regularly joined and sharply outlined

*b There is some free space between the seminal vesicles and the distal portion of the vas deferens

*c Ampulla of the seminal vesicles and ejaculatory ducts are clearly outlined down to the verumontanum and posterior urethra

*d Both seminal vesicles, their ampulla and ejaculatory ducts are almost symmetrical to the midline

GROUP 2 NONSPECIFIC INFECTIONS OF EPIDIDYMIS AND SEMINAL VESICLES

In chronic nontuberculous infections of the seminal tract

1 The convoluted tubule of the globus minor and in some cases the proximal end of the vas deferens are not adequately sharp and well outlined (fig 3, *B* left)

2 Some deviation of the distal end of the vas deferens may be present due to perivesiculitis and fibrosis (fig 5)

3 The ampulla of vas is hazy and ill-defined Also, it is drawn to and is incorporated with seminal vesicle (figs 3, *A*, 4 and 5) or sometimes with the opposite ampulla (fig 5)

4 Seminal vesicles are

*a Dilated and changed to a large, irregular and ill-defined sac (catarrhal vesiculitis) (figs 4, 5 and 12)

*b Irregular, scarred or alternately scarred and dilated with ill contour (figs 3, *A* and 5)

*5 The free space between the seminal vesicle and the ampulla of vas is partially or totally obliterated (figs 3, *A*, 4 and 5)

*6 Ejaculatory ducts may be obstructed and not visualized (fig 3, *A*) or incorporated with each other (fig 5)

* Pereira's interpretation

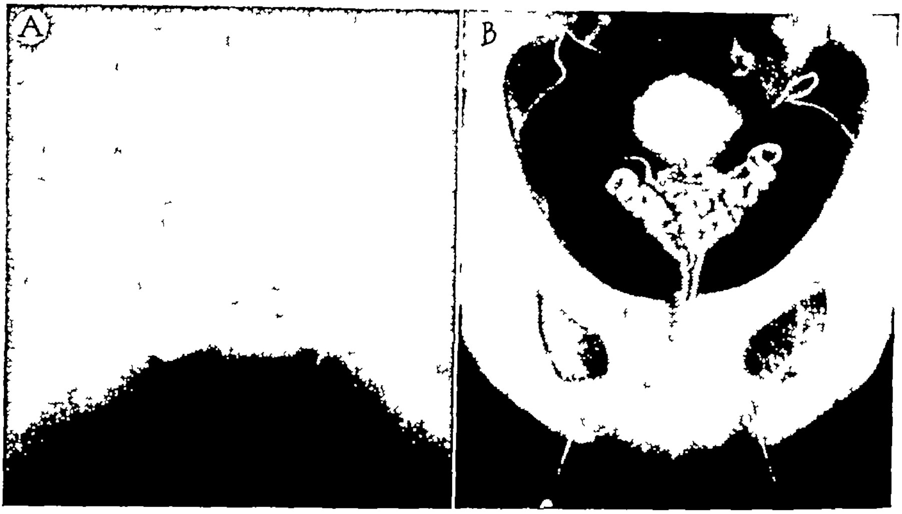

FIG 1 Case 1 M J , 24, No 20277 Clinical diagnosis Infectious hepatitis and normal genitourinary tract X-ray diagnosis Normal epididymides and seminal vesicles

paper on spermato-cystography in spinal cord injuries, Brodny and all[12] (1955) on the use of epididymography in genital tuberculosis

The purpose of this paper is to present an illustrated discussion on the x-ray findings in normal and six groups of patients showing some disorders of the seminal tract such as nonspecific infections, tuberculosis, obstructions, malignant changes, traumas and congenital malformations The material for this discussion is the selected cases from a series of more than 40 patients who have received not only this particular kind of investigation, but a complete urological and laboratory examination, particularly microscopic examination and culture of urethral discharge, prostatic secretion and semen

GROUP 1 NORMAL SEMINAL TRACT

In a normal epididymo-vesiculogram

1 The radiopaque medium does not pass proximal to the globus minor Rarely, the body of the epididymis is seen as a faint and hazy shadow (fig 6, *B* left)

2 The convoluted tubule of the globus minor as well as the proximal portion of the vas deferens is very thin and sharply outlined (figs 1, *A*, and 6, *B*)

3 Vas deferens is a sharp, thin, flexible and smooth tube from the globus minor of epididymis to the ampulla where it is irregular and slightly ill defined (figs 1, 2, and 4)

4 The shape of the seminal vesicles and their relation to the symphysis pubis are different from one case to another (figs 1 and 2) Also, in the same case, the shape and relation of vesicles would be different right at the time of injection of radiopaque medium and a few minutes or a few hours later (fig 2) However, right after injection of the radiopaque medium (figs 1, *B* and 2)

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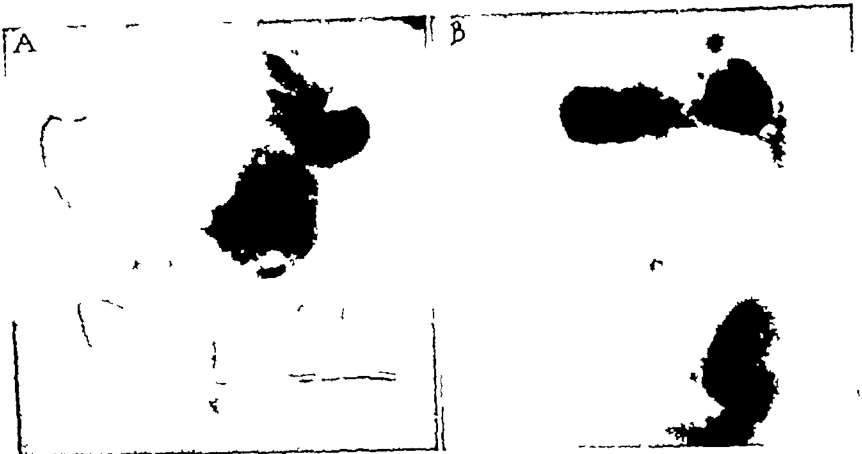

Fig 2 Case 2 H W , 20, No 15152 Clinical diagnosis Uveitis and normal genito urinary tract X ray diagnosis Normal seminal vesicles *A*, immediately after injection of opaque medium *B*, 10 minutes later

* a Seminal vesicles represent the confluence of a few or several small round or elongated saccules regularly joined and sharply outlined

* b There is some free space between the seminal vesicles and the distal portion of the vas deferens

* c Ampulla of the seminal vesicles and ejaculatory ducts are clearly outlined down to the verumontanum and posterior urethra

* d Both seminal vesicles, their ampulla and ejaculatory ducts are almost symmetrical to the midline

GROUP 2 NONSPECIFIC INFECTIONS OF EPIDIDYMIS AND SEMINAL VESICLES

In chronic nontuberculous infections of the seminal tract

1 The convoluted tubule of the globus minor and in some cases the proximal end of the vas deferens are not adequately sharp and well outlined (fig 3, *B* left)

2 Some deviation of the distal end of the vas deferens may be present due to perivesiculitis and fibrosis (fig 5)

3 The ampulla of vas is hazy and ill-defined Also, it is drawn to and is incorporated with seminal vesicle (figs 3, *A*, 4 and 5) or sometimes with the opposite ampulla (fig 5)

4 Seminal vesicles are

* a Dilated and changed to a large, irregular and ill-defined sac (catarrhal vesiculitis) (figs 4, 5 and 12)

* b Irregular, scarred or alternately scarred and dilated with ill contour (figs 3, *A* and 5)

* 5 The free space between the seminal vesicle and the ampulla of vas is partially or totally obliterated (figs 3, *A*, 4 and 5)

* 6 Ejaculatory ducts may be obstructed and not visualized (fig 3, *A*) or incorporated with each other (fig 5)

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* Pereira's interpretation

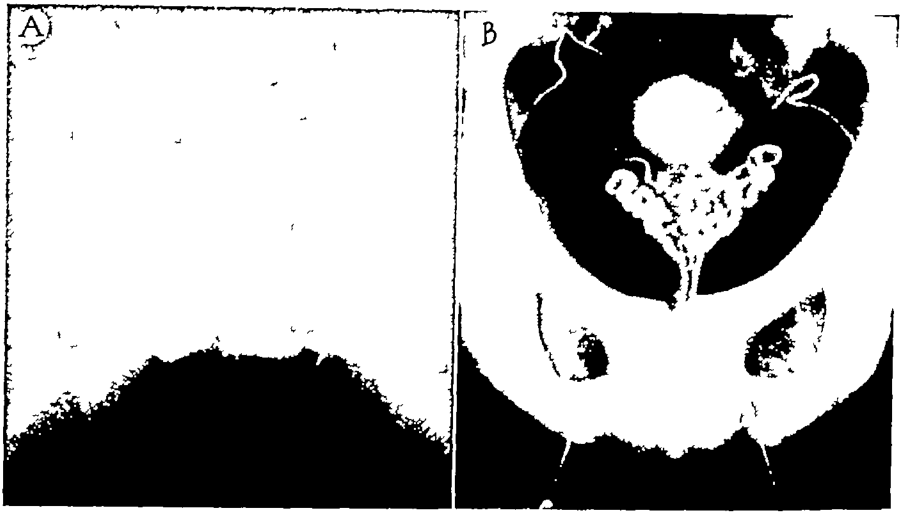

Fig 1 Case 1 M J , 24, No 20277 Clinical diagnosis Infectious hepatitis and normal genitourinary tract X-ray diagnosis Normal epididymides and seminal vesicles

paper on spermato-cystography in spinal cord injuries, Brodny and all[12] (1955) on the use of epididymography in genital tuberculosis

The purpose of this paper is to present an illustrated discussion on the x-ray findings in normal and six groups of patients showing some disorders of the seminal tract such as nonspecific infections, tuberculosis, obstructions, malignant changes, traumas and congenital malformations The material for this discussion is the selected cases from a series of more than 40 patients who have received not only this particular kind of investigation, but a complete urological and laboratory examination, particularly microscopic examination and culture of urethral discharge, prostatic secretion and semen

GROUP 1 NORMAL SEMINAL TRACT

In a normal epididymo-vesiculogram

1 The radiopaque medium does not pass proximal to the globus minor Rarely, the body of the epididymis is seen as a faint and hazy shadow (fig 6, *B* left)

2 The convoluted tubule of the globus minor as well as the proximal portion of the vas deferens is very thin and sharply outlined (figs 1, *A*, and 6, *B*)

3 Vas deferens is a sharp, thin, flexible and smooth tube from the globus minor of epididymis to the ampulla where it is irregular and slightly ill defined (figs 1, 2, and 4)

4 The shape of the seminal vesicles and their relation to the symphysis pubis are different from one case to another (figs 1 and 2) Also, in the same case, the shape and relation of vesicles would be different right at the time of injection of radiopaque medium and a few minutes or a few hours later (fig 2) However, right after injection of the radiopaque medium (figs 1, *B* and 2)

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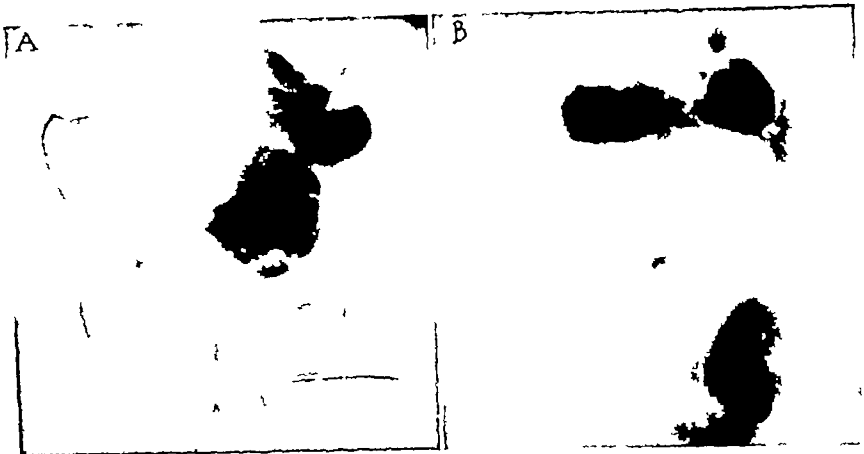
[12] Brodny, M L , Robins, S A , Hershman, H A and DeNuccio, A Epididymography, varicocelography, and testicular angiography Fertil & Steril , 6 158, 1955



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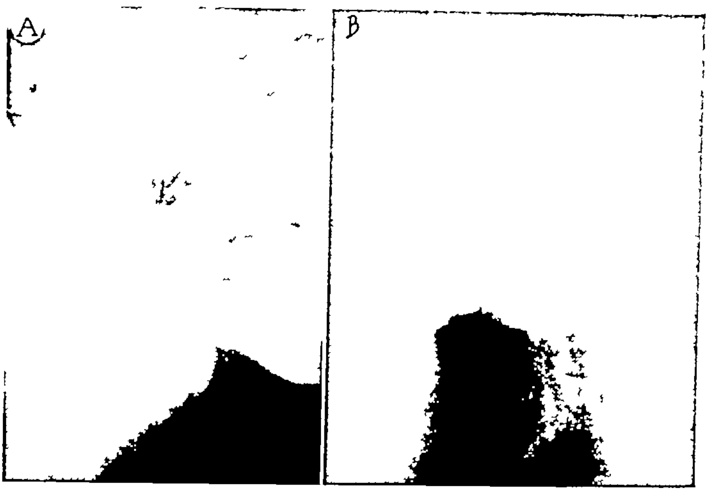

FIG 3 Case 3 W W, 26, No 20131 Clinical diagnosis Left epididymitis, prostatitis and seminal vesiculitis (Pseudomonas aerogenes) X ray diagnosis *A*, chronic seminal vesiculitis and perivesiculitis *B*, left epididymitis

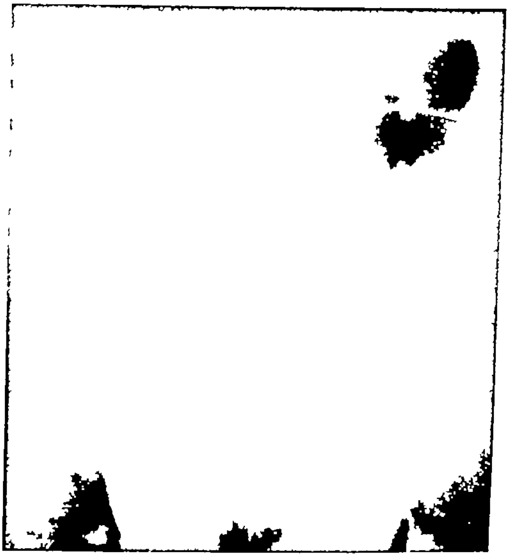

FIG 4 Case 4 H T, 26, No 24611 Clinical diagnosis Pyelonephritis, urethral stricture, prostatitis and seminal vesiculitis (gram positive cocci and alpha strep) X-ray diagnosis Catarrhal seminal vesiculitis

GROUP 3 TUBERCULOSIS OF SEMINAL TRACT

With careful study of the x-ray findings in this group of patients it seems that tuberculosis of the seminal tract would cause two different but combined roentgenographic disorders in this system (figs 6 and 7)

1 All the changes caused by chronic nonspecific infections of the seminal tract as fibrosis, dilation, distortion, obliteration, etc (See interpretation of group 2)

2 The characteristic destructive lesions of tuberculosis which show themselves

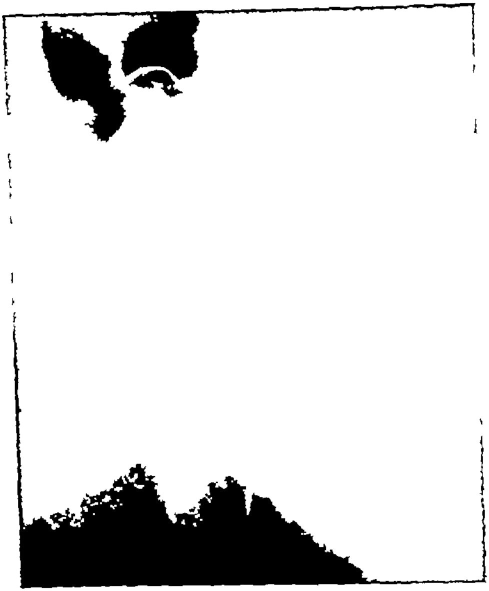

FIG 5 Case 5 J P 37 No 55116 Clinical diagnosis Recurrent right epididymitis prostatitis and seminal vesiculitis (Micrococcus hemolytic and nonhemolytic) Pathology report Non-specific epididymitis X ray diagnosis Seminal vesiculitis and perivesiculitis

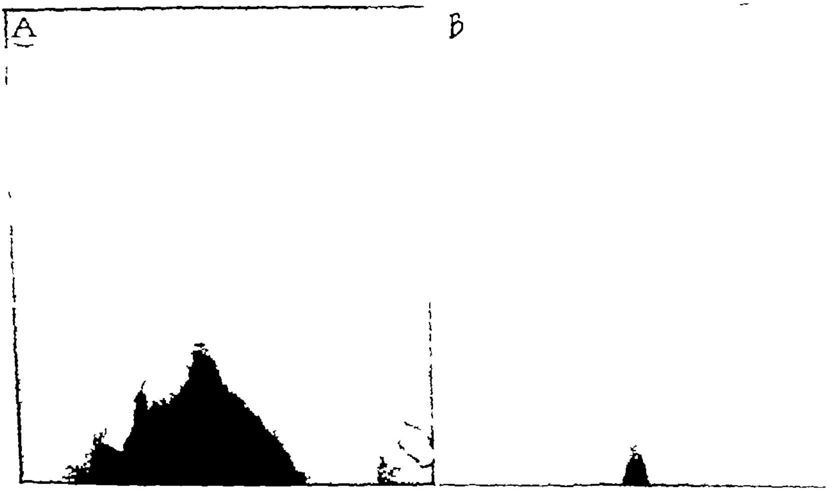

FIG 6 Case 6 J B J 29 No 58894 Clinical diagnosis Healed tuberculosis of lung recurrent right epididymitis and abscess of the right lobe of the prostate No acid fast bacilli were found in the urine Pathology report confirmed tuberculosis of the right epididymis X-ray diagnosis *A* chronic seminal vesiculitis and perivesiculitis associated with distortion of ampulla of right vas due to abscess of prostate *B* abscess of lower pole of right epididymis

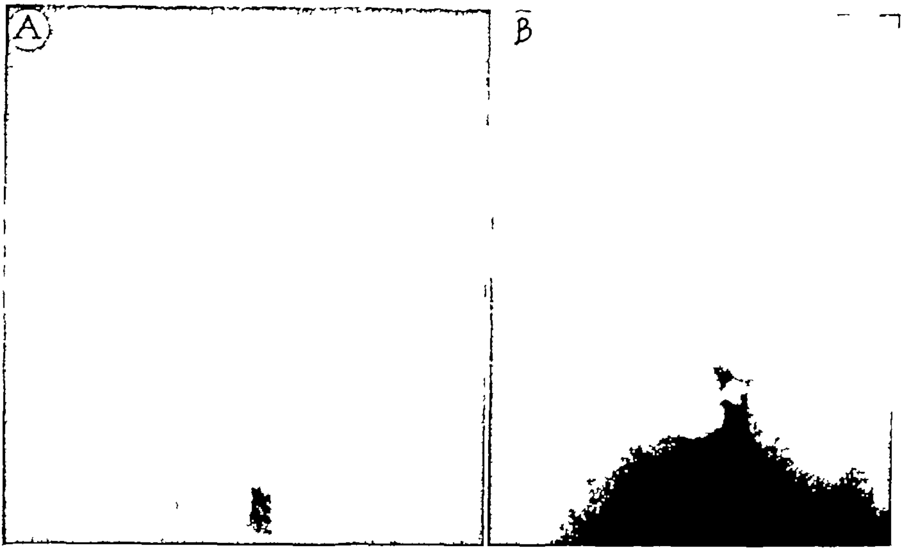

Fig 7 Case 7 W D, 50, No 68819 Clinical diagnosis Healed tuberculosis of lung Bilateral recurrent epididymitis, prostatitis and abscess of right seminal vesicle Urine positive for acid-fast bacilli Pathology report Tuberculosis of epididymides X ray diagnosis *A*, chronic seminal vesiculitis with abscess of the left vas *B* abscess cavity of lower pole of epididymis bilaterally

as abscess formation in the epididymis, vas deferens, seminal vesicles and the prostate or in two or three different parts of the seminal tract

GROUP 4 OBSTRUCTIVE LESIONS OF THE SEMINAL TRACT

The most common cause of obstruction of the seminal tract is the chronic infections of this system, and the most common sights of obstruction are the epididymis (especially the tail), ampulla of the vas deferens and ejaculatory ducts However, the result of this obstruction which may be due to stricture, exudate and pus formation or both (as in our case) is azospermia and sterility

In these cases the injected radiopaque medium stops completely at the region of obstruction (complete obstruction) (figs 8 and 11) or passes a narrow and tight section of the vas deferens or ejaculatory duct (incomplete obstruction) (fig 3, *A*)

GROUP 5 METASTATIC TUMORS OF THE SEMINAL TRACT

As figures 9 and 10 demonstrate, metastatic tumors of the seminal vesicles, ejaculatory ducts and ampulla of the vas provide the same roentgenographic changes as the chronic infections of this system do Rectal examination of the prostate and biopsy would be a great help for the correct interpretation and diagnosis

GROUP 6 TRAUMATIC LESIONS OF THE SEMINAL TRACT

Epididymitis after scrotal surgery, division of the vas in orchi-epididymectomy or in prostatectomy and also tearing of ejaculatory ducts and verumontanum at time of enucleation of the prostate are the most common types of surgical trauma to the seminal tract Accidental trauma to this system is rare

Here in our case (fig 11), due to removal of verumontanum and ejaculatory

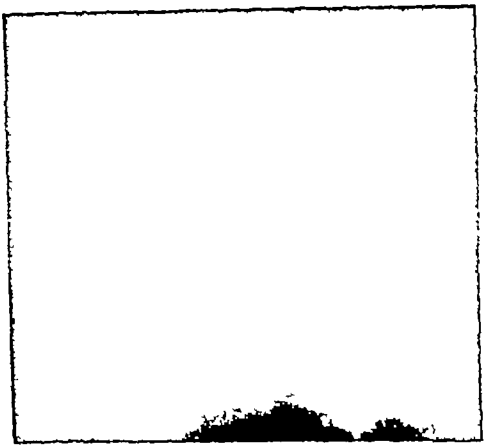

Fig 8 Case 8 O H, 40, No 229297 Clinical diagnosis Azospermia, prostatitis and seminal vesiculitis (history of gonorrhea and bilateral epididymitis at the age of 19) Testicular biopsy was normal X ray diagnosis Catarrhal seminal vesiculitis, complete obstruction of left vas and proximal portion of right

Fig 9 Case 9 M W, 71, No 19464 Clinical diagnosis Adenocarcinoma of prostate invading seminal vesicles and metastatic carcinoma of lungs X ray diagnosis Distortion of ampulla of left vas, obliteration of left ejaculatory duct and part of right seminal vesicle

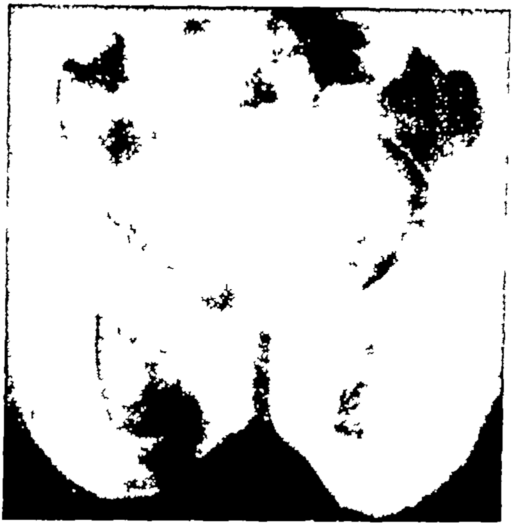

Fig 10 Case 10 R A , 45, No 49638 Clinical diagnosis Adenocarcinoma of prostate invading seminal vesicles and bony metastasis X ray diagnosis Deviation of ampulla of left vas to midline, obliteration and irregularity of both vesicles and obstruction of left ejaculatory duct and ampulla of seminal vesicle

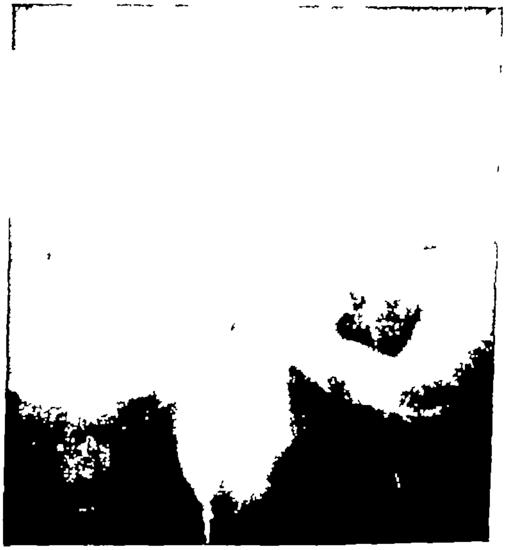

Fig 11 Case 11 H J , 73, No 57464 Clinical diagnosis Benign prostatic hypertrophy plus chronic prostatitis and seminal vesiculitis X ray diagnosis Torn ejaculatory ducts chronic left seminal vesiculitis and obstruction of right vas

ducts at the time of prostatectomy, a pooling of dye is seen in the posterior urethra The normal ampulla of seminal vesicles as well as ejaculatory ducts (figs 1, 1 and 2) cannot be seen

GROUP 7 CONGENITAL ABNORMALITIES OF SEMINAL TRACT

Polyorchism, double epididymis and bifid vas deferens have been seen and reported In figure 12, a rare abnormality of the seminal vesicles is illustrated

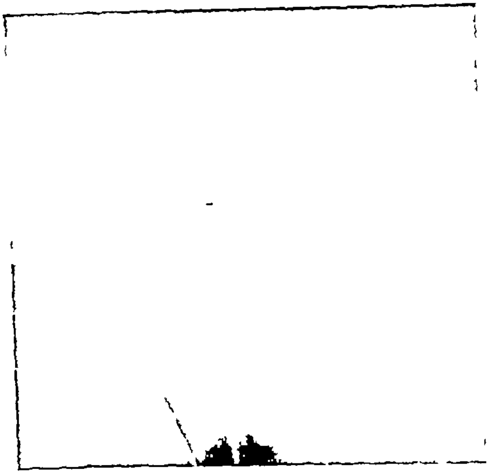

FIG 12 Case 12 I S 38, No 235882 Clinical diagnosis Chronic prostatitis and seminal vesiculitis associated with bloody ejaculation (No acid fast bacilli but gram positive cocci) X ray diagnosis Chronic catarrhal seminal vesiculitis and bilateral double seminal vesicles

Considering the overall picture of a normal epididymo-vesiculogram (figs 1 and 2) the interpretation of a supernumerary epididymis, vas deferens or seminal vesicles is simple, whereas the diagnosis of an agenesis from obstruction may need surgical exploration

Methods of epididymo-vesiculography Belfield vasotomy and Luys vasopuncture were the only means for seminal vesiculography until Young and Luys employed catheterization of the ejaculatory ducts through a direct panendoscopy which made the retrograde catheterization of the ejaculatory ducts much easier However, the review of the literature and personal experience reveal the original Belfield vasotomy is the simplest means [13, 14]

Technique of seminography includes the following steps

1 Prepare and drape the patient on the x-ray table and in supine position

2 Under local anesthesia with 1 per cent novocain solution, expose about 2 cm of the vas bilaterally at 4 to 5 cm below the external inguinal ring

3 Insert the total length of a No 20 or 21 gauge round tip hypodermic needle into the lumen of the vas toward seminal vesicle through a longitudinal incision about 2 mm long

4 Inject 1½–2 cc of radiopaque medium (we use 70 per cent solution of urokon) slowly, continuously and without force through the needle into each seminal vesicle It is not necessary to tie the vas around the needle

5 Take one x-ray film (with Bucky) right at the end of injection when the symphysis pubis is on the center of the plate

6 Remove the needles and reinsert them into the vas, toward epididymides

7 Inject 0 3–0 5 cc of the radiopaque solution through the needle into each

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[13] Gambetta G and Bonini L La vésiculographie dans la tuberculose genitale, notre expérience personnelle et présentation de dix radiogrammes Acta urol belg 23 285, 1955

[14] Belfield W T Pus tubes in the male and their surgical treatment J A M A , 44 1277 1905

epididymis under gentle pressure To prevent extravasation of dye, it is advisable to use an insulin or tuberculin syringe (long and thin with 1 cc capacity) and inject the medium without force Here, one may need to tie the vas temporarily around the needle

8 Take one x-ray film (without Bucky) right at the end of injection The plate is a cardboard covered film which is localized under the buttocks The patient's legs are in abduction and the scrotum is over the center of plate

With turning the patient on prone position epididymogram may be more obvious and clear (Abeshouse), but care must be taken not to contaminate the wound

9 Remove the needles, release the vas, put a skin suture on the scrotum and apply a temporary dressing Be sure no bleeding point is left untied

COMPLICATIONS

Transection or crushing the vas, hematoma or infection in the scrotal sac and obstruction of the vas due to scarring and fibrosis are the possible complications

SUMMARY

In March 1913, Belfield advised roentgenographic examination of the seminal vesicles through a vasotomy opening using a 5 per cent collargol solution as radiopaque medium Since then, and after May 1952, when Boreau, et al published a paper on x-ray examination of the epididymis, the subject of seminography and the clinical application of it have been matters of investigation and discussion

Reviewing the literature and considering the positive findings in the reported cases, the roentgenography of the seminal tract in normal and pathological conditions may be interpreted as follows

1 Normally (figs 1 and 2) The convoluted tubule of the globus minor of the epididymis and the vas deferens is thin, sharply outlined and flexible in appearance The ampulla of vas is slightly irregular and located about 1 5–2 mm above and medial to the seminal vesicle which itself is sacculated and well defined Finally the ampulla of seminal vesicle and ejaculatory duct are well visualized

2 In nonspecific infections (figs 3, 4 and 5) The convoluted tubule of epididymis is hazy and ill-defined The ampulla of vas may be incorporated with seminal vesicle which itself is scarred or dilated Ejaculatory duct may be obstructed

3 In tuberculosis (figs 6 and 7) The radiographic changes are similar to those seen in nonspecific infections, but accompanied with abscess formation

4 In obstructions (figs 3, 8 and 11) The lack of filling of the seminal tract, distension of seminal vesicle or nonvisualization of the ejaculatory duct is impressive

5 In metastatic tumors (figs 9 and 10) The changes are the same as chronic infections, but physical examination and biopsy will provide the final answer

6 In traumas (fig 11) The x-ray findings of obstruction due to scarring or ligation and the pooling of dye in posterior urethra as the result of disruption of ejaculatory ducts are important

7 Congenital abnormalities (fig 12) Considering the normal epididymo-

vesiculogram the diagnosis of supernumerary organs is not a problem whereas a correct interpretation of the lack of the radiographic picture may necessitate a surgical exploration

COMMENTS

Considering the foregoing, one may be justified to say that much more study has to be done to make seminography a routine procedure for seminal tract evaluation It is undeniable that roentgenographic examination of seminal tract is an important and essential step in investigation of the sterility problems The value of such examination in other types of seminal tract disturbances depends on the further successful studies and additional careful interpretations

ACKNOWLEDGMENT

I must make my sincere acknowledgment to Dr Donald J Jaffar associate professor of urology Wayne University College of Medicine whose help made possible for me to start this piece of work and study at Receiving Hospital and whose permission for presentation of those cases in this paper is greatly appreciated Also I gratefully thank Drs Maitland Stewart, Henry Domzalski George Sewell Jr Frank Schwarz and Robert Lutton who were kind enough to let me apply this procedure on their private cases and who aided me during the performance of the procedures

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PREVENTION OF POSTOPERATIVE STRICTURE FROM TRANSURETHRAL RESECTION BY PRELIMINARY INTERNAL URETHROTOMY REPORT OF EXPERIENCE WITH 447 CASES*

JOHN L EMMETT, DIETER KIRCHHEIM AND LAURENCE F GREENE

From the Section of Urology, Mayo Clinic and Mayo Foundation, Rochester, Minn

In May 1953, one of us, with Winterringer,[1] [2] presented a preliminary report on his experience with internal urethrotomy as a means of preventing stricture resulting from transurethral resection The report comprised 59 cases in which urethrotomy was done with the Otis urethrotome during the year May 1952, through April 1953 Since January 1, 1953, preliminary calibration of the urethra with Otis bulbs and internal urethrotomy with the Otis urethrotome, when indicated, has been practiced routinely on the transurethral surgical services of Drs Emmett, Greene and DeWeerd of the urologic staff of the Mayo Clinic This report deals with this combined series of cases and also includes data on the 59 cases presented in the preliminary report

Our combined experience has convinced us of the superiority of Otis diagnostic bulbs (bougie à boule) over steel sounds for accurate calibration of the meatus, fossa navicularis, pendulous urethra, penoscrotal juncture and region immediately proximal We believe that minimal degrees of narrowing, as well as the exact size and length of the narrowed area, can best be determined with bulbs Calibration of the bulbomembranous urethra is best done with steel sounds

TECHNIQUE

Calibration of the urethra No 26, 28 and 30F Otis bulbs (fig 1) are part of the instrumental "setup" for each transurethral resection The bulb is carefully and slowly passed through the anterior urethra until its tip rests easily in the perineal urethra or distal part of the bulb of the urethra No attempt is made to pass it through the bulb of the urethra and into the membranous urethra The slightest "jump," "hang" or resistance with any bulb is considered an indication for urethrotomy If the 26F bulb will not pass the meatus, *meatotomy* with the Otis urethrotome to 32F as described by Greene[3] is done, and then calibration of the urethra is continued In the occasional case with a very narrow urethra it is, of course, necessary to calibrate with smaller bulbs (8 to 24F) The calibration should be done carefully and slowly, otherwise minimal degrees of narrowing may not be appreciated

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* Abridgment of paper read at the meeting of the North Central Section of the American Urological Association, Cleveland, Ohio, October 3 to 5, 1956 and published in full in the Transactions of the North Central Section of the American Urological Association, pp 177–191, 1957

[1] Emmett, J L and Winterringer, J R Urethral stricture following transurethral resection prevented by internal urethrotomy Preliminary report of experience with Otis urethrotome Tr Am A Genito Urin Surg , **46** 12–25, 1953

[2] Emmett, J L and Winterringer, J R Urethral stricture following transurethral resection prevented by internal urethrotomy Preliminary report of experience with Otis urethrotome (Abridged version) J Urol **72** 867–874, 1954

[3] Greene, L F External meatotomy Urologist s Correspondence Club Letter March 7, 1955

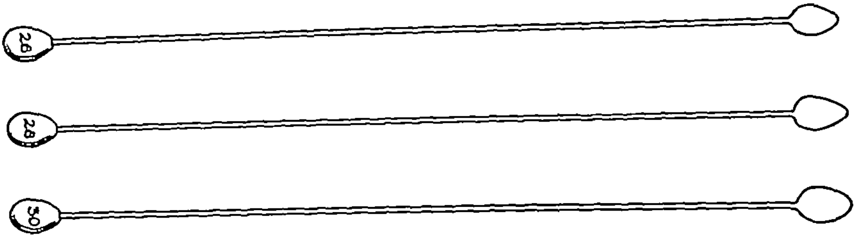

FIG 1 Otis diagnostic bulbs (bougie à boule)

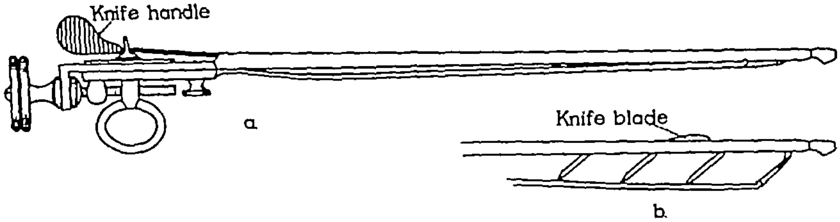

FIG 2 Otis urethrotome, straight model Tip of instrument is equipped with screw threads for attachment to filiform guide if desired In this illustration a small metal tip has been screwed on so that instrument can be used without filiform guide

Urethrotome We employ only the straight-model Otis urethrotome (fig 2) We do not use the curved model, since we do not want it to enter the bulbomembranous urethra

Meatotomy (technique) As mentioned by Greene,[3] narrowing of the so-called urethral meatus often is not situated at the meatus, but is farther proximal in the fossa navicularis At times it may be at the most proximal part of the fossa, at its junction with the pendulous urethra It may be most difficult to cut accurately in the conventional manner with a scalpel in this region We have found that cutting with the Otis urethrotome is a much more satisfactory procedure Apparently it makes little difference whether the cut is made in the roof (12 o'clock position) or floor (6 o'clock position) of the fossa We have employed the former site in most of our cases, whereas White and Berry[4] turn the urethrotome upside down and cut at the 6 o'clock position The instrument is introduced a distance of about 3 cm and expanded to 32F and the cut is made as for urethrotomy described later If the meatus and fossa are very narrow, the expansion of the instrument is done in multiple stages, making successive cuts until a caliber of 32F is achieved This prevents forceful dilatation of the meatus, which will result in stricture This procedure results in fewer "fish-mouth" meatuses and postoperative meatal strictures than is the case when the conventional type of meatotomy is done

Urethrotomy The Otis urethrotome is inserted into the urethra in its closed position with the dial and knife slot pointing upward (12 o'clock position of the urethra) (The instrument should be inspected closely before it is used to be sure that the dial reads 15F when it is completely closed) The instrument is passed gently and slowly until the tip rests lightly in the perineal (or distal

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[4] White, E P and Berry N E Personal communication to the authors

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Of the 447 cases, we have followup data on 353 cases (79 per cent). Of these 353 cases, in 292 (83 per cent) the length of followup was 1 year or more, whereas in 61 (17 per cent) the followup interval was from 6 to 12 months.

Preoperative data. Variation in caliber of the "normal adult male urethra." If the 43 patients treated primarily for urethral stricture are excluded, a total of 404 patients are left in whom internal urethrotomy was done as a preliminary procedure for transurethral operation. An analysis of the preoperative calibration in these cases is interesting. In 345 cases the caliber of the urethra was 26 to 30F. (26F caliber means that slight resistance can be detected with the 26F bulb but none with the 24F bulb.) In 59 cases the caliber was 24F or less. In the 345 cases with a caliber of 26F to 30F, no history could be elicited (except in three cases) of urethral disease or trauma which might predispose to urethral narrowing, a fact which leads us to the conclusion that calibers of 26F or larger can be considered variations of normal.

The problem of the 59 cases with a urethral caliber of 24F or less presents a more difficult situation to appraise. Of these 59 cases preoperative urethral calibration was as follows: 24F, 19 cases; 22F, 10 cases; 18 to 20F, 15 cases; 12 to 16F, 11 cases; and 0 to 10F, four cases.

Of the 19 cases with a urethral caliber of 24F no history of previous disease or trauma which might predispose to stricture could be elicited in 12. Of the remaining seven, six had had previous transurethral resection and one had had many previous urethral instrumentations for fulguration of recurring vesical tumor. These data suggest to us that about two-thirds of male urethras which calibrate at 24F (especially in patients with no history of previous instrumentation or urethral disease) can be classed as variations of normal.

The situation with urethras of 22F caliber presents quite a different picture. Of the 10 cases in this category, the history disclosed a definite reason for stricture in eight. In the other two the history was incomplete in this respect. This

TABLE 1. *Results of preoperative calibration of the adult male urethra in 1,824 patients who underwent transurethral operation*

Caliber	Cases	Percentage of Total (1,824 Cases)
More than 30F*	1,420	77.8
30F†	120	6.6
28F‡	116	6.4
26F	109	6.0
24F§	19	1.0
22 to 8F	40	2.2

* Since a 30F bulb met no resistance, internal urethrotomy was not done.

† A 30F bulb met slight resistance, but a 28F bulb passed easily.

‡ A 28F bulb met slight resistance, but a 26F bulb passed easily.

§ Seven of these patients had pathologic stricture.

All pathologic strictures.

part of the bulbous) urethra (Care should be taken that the tip of the instrument does not inadvertently slip into the membranous urethra or prostatic urethra, thereby endangering the external sphincter when the cut is made)

The object of the procedure is to make a clean linear cut in the roof (12 o'clock position) of the urethra to 36F without avulsing or overstretching the urethra To do this, the instrument is expanded slowly and carefully until it is just comfortably snug, following which the knife is withdrawn through the entire length of the urethra, with a brisk, determined motion, so that it will cut cleanly (Because the blade is not sharp, it will cut only the narrow areas in which the urethra is stretched tightly against the knife) If the cut is less than 36F, the blades are closed, the knife is returned to the "home" position and the procedure is repeated until the final cut has been made with the urethrotome blades expanded to 36F Following the urethrotomy a 30F Van Buren sound is passed into the bladder to calibrate the bulbomembranous and prostatic urethra The resectoscope is then passed gently

Postoperative care After the resection is completed, a 26F two-way irrigating Foley bag catheter is left indwelling for 72 hours The catheter provides pressure for hemostasis, and allows the incision in the urethra to seal over and partially heal before the patient voids through it This procedure, plus the administration of a broad spectrum antibiotic for 24 hours preceding and 5 or 6 days following operation, has apparently been an effective factor in preventing febrile reactions Febrile reactions have been no more frequent after transurethral operations in which internal urethrotomy was done than after those in which internal urethrotomy was not necessary

EXPERIENCE WITH 447 CASES IN WHICH INTERNAL URETHROTOMY WAS PERFORMED

Material From May 1, 1952, to January 1, 1956, 447 internal urethrotomies have been done on the transurethral surgical services of Drs Emmett, Greene and DeWeerd Of these, 404 were done as preliminary procedures to transurethral operations (381 for transurethral resection of the prostate or vesical neck, 11 for combined prostatic resection and removal of vesical tumor, 11 for removal of vesical tumor only, and one for litholapaxy only) The remaining 43 were done solely for treatment of urethral stricture It is of interest that these 404 cases represent an incidence of about 22 per cent of the transurethral operations done on the three services during this period (approximately 1,824 cases) This figure agrees fairly closely with the 20 per cent incidence reported in the preliminary report and also with Nesbit's experience that external perineal urethrotomy was required in 20 per cent of his patients who underwent transurethral resection

Length of followup It is our opinion that postoperative stricture or recontracture of a pre-existing stricture becomes apparent in most cases within 6 months Certainly it may be said that almost 100 per cent of postoperative strictures become apparent within 1 year after operation For this reason we have not included any postoperative data on less than a 6-month followup Also, all data of 1 year or more (even though the followup interval is 2 or 3 years) have been grouped together under the heading "1 year or more followup " Thus, we have a larger one, but assume that the urethra is quite normal. This was the case in 44 patients. In six patients the only data we have are the result of a cystoscopic examination (usually followup for vesical tumor), in which a 22F cystoscope is used routinely. In seven patients home physicians passed sounds (usually being conservative in the size used). We simply have the data in these cases that a sound passed easily, the size varying from 18 to 28F. As a result of these data we conclude that in 57 patients the caliber of the urethra was quite normal (26F or more). In only three cases did we discover any reduction in caliber, as follows: two cases, 22F, and one case, 18F.

As for the "implied data," we estimate that the urethral calibration must be normal or near normal in 206 patients and questionable in only four. Our reason for this conclusion is as follows: 37 patients returned to the clinic for other reasons but, since there were no urinary symptoms and the urine was negative, were never seen in the Section of Urology, therefore, no calibration was done. One hundred and fifty-two patients reported by letter that they voided without difficulty, with a good stream, and had no urinary symptoms. Seventeen patients stated that they were having difficulty voiding, but it seemed quite evident from the description they gave that their difficulty was on the basis of recurring obstruction of the vesical neck rather than urethral narrowing. Four letters were impossible to evaluate.

From these data we conclude that the results of internal urethrotomy for the purpose of enlarging a "normal" urethra (of 26 to 30F caliber) to 36F to prevent postoperative stricture from transurethral resection are extremely satisfactory. Apparently, postoperative stricture is extremely rare if careful preoperative calibration is done and internal urethrotomy is performed when indicated. It is our opinion (as expressed in the preliminary report) that in this group of cases the caliber of the urethra no doubt returns to its normal preoperative size.

Data in patients whose urethras were of 24F caliber or less. There was a total of 59 patients in this group, of whom we have followup data on 50. Of the 50, followup data were obtained by return visits in 17, and from followup letters in 33. Adequate calibration has been maintained, sufficient to keep the patient asymptomatic, in 41 of the 50 patients followed (82 per cent). *Adequate postoperative calibration data* are available for only 14 of the 50 patients followed. Of these 14, the postoperative urethral caliber was greater than the preoperative caliber in all cases (26F or larger in eight).

RESULTS OF INTERNAL URETHROTOMY FOR STRICTURE OF THE ANTERIOR URETHRA

Urethrotomy for both "stricture only" and for stricture complicating the performance of transurethral resection. Preoperative data. Referring again to the group of 59 cases with urethral caliber of 24F or less, in which internal urethrotomy was done as a preliminary procedure for transurethral resection, it will be recalled that we concluded that 47 were the result of definite stricture. It should now be helpful to combine these 47 cases with the 43 cases in which treatment was for stricture only, so that we may get a better picture of the results of internal urethrotomy for stricture. This gives us a combined group of 90 cases of stricture leads us to the conclusion that most urethras of 22F caliber should be classed as strictured (either acquired or congenital), rather than a variation of normal It is quite obvious that urethras of smaller caliber (20F or less) must be considered as strictured

An analysis of the calibration of the adult male urethra in approximately 1,824 patients who underwent transurethral operation is shown in table 1

RESULTS OF INTERNAL URETHROTOMY DONE AS A PRELIMINARY PROCEDURE FOR TRANSURETHRAL OPERATIONS

Data in patients whose urethras were of "normal" caliber (26 to 30F) There was a total of 345 patients in this group, of which we have followup data on 270 Of the 270, followup data were obtained from return visits in 90 cases and from followup letters in 180 Results (table 2) are classified in two categories, "accurate calibration data" and 'implied data " Regarding the 'accurate calibration data" it will be noted that postoperative calibration was done in 60 patients (all except seven done at the clinic) To avoid unnecessary pain, it has been our custom to pass only a 26F Van Buren sound If it passes easily, we do not pass

TABLE 2 *Results of internal urethrotomy to enlarge the urethra preliminary to transurethral resection in 270 male patients with "normal" caliber of urethra (26 to 30F) for whom followup data are available*

A Preoperative calibration maintained or increased in 263 cases

Data from Accurate Calibration (57 Cases)		Implied Data (206 Cases)	
Details of calibration	Cases	Classification	Cases
26F sound or larger passed easily	44	Returned to clinic but not seen in Section of Urology because no urinary symptoms and urine negative	37
22F cystoscope (only) passed easily	6	From letter Patient voids normally—no urinary symptoms	152
Sounds passed by home physician No obstruction encountered Sounds varied in size from 18 to 28F	7	From letter Patient voids with difficulty, but due to vesical neck	17
Total	57	Total	206

B Preoperative calibration *not* maintained or followup data impossible to evaluate in 7 cases

Data from Accurate Calibration (3 Cases)		Implied Data (4 Cases)	
Details of calibration	Cases	Classification	Cases
22F caliber 18F caliber	2 1	Letter impossible to evaluate	4
Total	3	Total	4
Grand total	60	Grand total	210

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TABLE 3 *Cause of stricture in 90 patients treated by internal urethrotomy*

Cause	Cases
Previous transurethral resection	46
Other instrumentations	9
Neisserian urethritis	15
Trauma	3
Congenital	2
Not known	15
Total	90

TABLE 4 *Results of internal urethrotomy in 72 patients with stricture of the urethra who have been followed**

A Adequate calibration maintained or sufficient to keep patient asymptomatic in 48 cases (67 per cent)

Data from Accurate Calibration			Implied Data	
Postoperative caliber	Preoperative caliber	Cases	Classification	Cases
26F or larger	24F	2	Return visit Voids well, no symptoms, not calibrated	3
26F or larger	22F	2		
26F or larger	20F	2	By letter Voids without difficulty, no symptoms	24
26F or larger	18F	1		
26F or larger	12F	1	By letter Voids poorly but due to vesical neck	2
26F or larger	8F	1		
22F cystoscope easily	?	1		
22F cystoscope easily	20F	4		
22F cystoscope easily	18F	2		
22F sound easily	22F	1		
22F sound easily	16F	1		
22F sound easily	12F	1		
Total		19	Total	29

B Adequate calibration *not* maintained, stricture recontracted in 24 cases (33 per cent)

Data from Accurate Calibration	Cases	Implied Data by Letter	Cases
Return visit Periodic dilatation necessary	4	Periodic dilatation necessary	15
		Occasional dilatation necessary	2
		"Having trouble with stricture"	1
		Impossible to evaluate letter	2
Total	4	Total	20

* In 39, urethrotomy was done to permit transurethral resection, in 33 it was done for treatment of stricture only

for study From table 3 it can be seen that more than 60 per cent are the result of previous transurethral resection or other urethral instrumentation The site of the strictures is almost equally divided between the pendulous urethra (47 cases) and the penoscrotal juncture (43 cases) The caliber of the strictures is as follows 0 to 10F, eight cases, 12 to 16F, 40 cases, 18 to 20F, 19 cases, 22F, 12 cases, 24F, nine cases, and not stated in two cases It will be noted that more than 50 per cent were of 16F or less

Results of urethrotomy The results of urethrotomy for stricture are given in table 4 Of the 90 cases of stricture, 72 have been followed (45 by letters and 27 by return visit) Adequate calibration sufficient to keep the patient asymptomatic, has been maintained in 48 cases (67 per cent), while in 24 (33 per cent) calibration has not been maintained and periodic or occasional dilatation is required We have been unable to detect any reason why in some cases the urethra should remain of good caliber and in others it should recontract

Efficacy of use of prolonged indwelling urethral catheter postoperatively Doss[5] has suggested the use of an indwelling 26F Foley catheter for several weeks following urethrotomy, as a means of preventing or delaying recontracture of the stricture Our patients have been intolerant to the wearing of a 26F catheter, but 16 patients have succeeded in wearing a 24F catheter for varying periods of 1 to 6 weeks postoperatively Twelve of these patients have been followed The preoperative calibration of the 12 strictures was 8F, two cases, 10F, two cases, 14F, one case 16F, six cases, and 22F, one case Five of the twelve patients still require periodic dilatation, one requires occasional dilatation, while the remaining six have stated in their letters that they void without difficulty and have no urinary symptoms There seems to be no correlation between the postoperative caliber of the stricture and the length of time the catheter was worn As a matter of fact, the three patients who wore the catheter for the longest period (5 to 6 weeks) still require periodic dilatation Comparing the results of this group of 12 patients with those of the entire group of patients who had strictures, there appears to be no striking improvement in results from the prolonged use of an indwelling catheter

COMPLICATIONS OF INTERNAL URETHROTOMY

In the preliminary report[1] attention was called to the fact that internal urethrotomy was more or less abandoned shortly after the turn of the century because of the serious complications of *sepsis, extravasation, hemorrhage* and *chordee* The paucity of postoperative complications in our series of cases is, we believe, due to several factors 1) We have limited the procedure to the anterior urethra (Most serious complications arose from urethrotomy performed in the deep, unprotected bulbomembranous urethra) 2) The operations are done only in the hospital operating room, under aseptic conditions, and a large indwelling catheter is left in place for a full 3 days Also broad spectrum antibiotics are given preoperatively and postoperatively 3) Strictures of the present day are not the extensive, dirty, long-standing, badly infected strictures that were so prevalent 50 years ago In more than three-fourths of our cases no urethral stricture was present

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[5] Doss A K Personal communication to the authors

Hemorrhage and extravasation Complications following internal urethrotomy in this series of cases have been surprisingly few We have not encountered any case of extravasation or any severe postoperative bleeding In two or three cases, because of slightly excessive bleeding, an elastoplast bandage, exerting compression against the 26F indwelling catheter, has been sufficient for control We believe that the presence of the large urethral catheter for 72 hours is a great help in the prevention of hemorrhage We have encountered an occasional patient in whom moderate urethral bleeding occurred a few days after leaving the hospital In all of these cases bleeding was promptly controlled with an indwelling catheter which was left indwelling for 24 to 72 hours

Fever and sepsis Postoperative fever and sepsis attributable to internal urethrotomy have been almost nonexistent

Epididymitis There have been five cases of postoperative epididymitis in this series of 447 cases, which is about the normal incidence (approximately 1 per cent) for all of our transurethral resections (We do not employ routine bilateral vasoligation preliminary to transurethral resection)

Thrombophlebitis The incidence of thrombophlebitis has not increased as a result of preliminary urethrotomy

Chordee The only complication that has given us any concern is the appearance of chordee (*downward* curvature of the penis with erection) in four cases (an incidence of a little less than 1 per cent of the series) In two of these patients, aged 63 and 69 years, the pendulous urethra calibrated at 26F Internal urethrotomy was done to enlarge the urethra preliminary to transurethral resection One of these patients returned to the clinic 1 year after operation A 26F sound passed easily and the patient voided freely The penis and the urethra were entirely normal to palpation, *including palpation against a sound in the urethra* The second patient has not returned He reported the chordee by letter The third patient is a man aged 47 years, who had a severe stricture of the distal third of the pendulous urethra which would not respond to dilatation and kept up a more or less constant hemorrhagic and purulent discharge Urethrotomy has improved the situation so that periodic passage of sounds keeps the urethra dilated easily to 28F (whereas previously 16F was the maximum) The patient has moderate chordee on erection, but is able to consummate coitus satisfactorily without pain and does not complain about it *Palpation of the penis and urethra* also is entirely negative The fourth patient is a man 63 years of age, who required relief for prostatic obstruction by transurethral resection Because of an ancient traumatic stricture (20F situated at the penoscrotal juncture), internal urethrotomy was done to admit the resectoscope, which moved freely in the urethra during the entire resection By letter the patient reports that he now voids an excellent stream, has clear urine and no urinary symptoms, but complains rather bitterly about the downward curvature of the penis on erection An excerpt from his letter seems to sum up the problem quite well, as follows

"A condition of this kind is of minor importance to a man of my age, but doubt that a young fellow would be at all pleased with like results"

The mechanism of chordee following urethrotomy is not entirely clear to us, especially in the absence of any palpable lesion in the urethra or corpora If the incidence of this complication, however, proves to be only about 1 per cent, we feel that it is a small price to pay to prevent postoperative urethral stricture Also, most urologists have encountered patients who complain of upward curvature (as seen in Peyronie's disease) following transurethral resection in which no urethrotomy has been done In some of these cases fibrous plaques can be palpated while in others they cannot

Resectoscope becoming snug in urethra during transurethral resection, in spite of apparently adequate preoperative caliber In nine cases in this series of 447, in spite of an apparently adequate urethra (30F bulb passed easily), the resectoscope became snug in the urethra" within 10 or 20 minutes after resection began It is our feeling that in these cases we were not careful enough in the preoperative calibration Quite likely the bulb was passed too rapidly to detect a minimal degree of narrowing In all cases the resectoscope was removed, internal urethrotomy was done, and the resection was completed A followup of eight of these cases (four return visits and four followup letters) shows normal calibration in three cases and no urinary symptoms or urethral narrowing in the others

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THE UPPER URINARY TRACT IN ADVANCED PROSTATIC CARCINOMA

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It is well known that in patients with prostatic carcinoma the upper urinary tract may suffer damage from back pressure either as a result of bladder neck obstruction or of constriction of the ureter from trigonal infiltration or secondary to invasion of the fascia surrounding the seminal vesicle on one or both sides[1]

Although investigation of the upper urinary tracts by pyelography is generally considered an essential part of the diagnostic study of patients harboring prostatic malignancy, there is available in standard urological texts a paucity of information regarding the incidence and type of upper urinary tract disease in patients with advanced prostatic carcinoma except for postmortem studies such as those of Graves and Militzer[2] and Mintz and Smith[3] While several reports[4, 5] have appeared dealing with the influence of anti-androgenic treatment on 5-year survivorship, there has been little information available on the subject of the fate of the upper urinary tracts following anti-androgenic treatment in advanced prostatic carcinoma

The subject of the status of the upper urinary tracts is of more than academic interest, since in a previous communication[5] from this clinic it was shown that the condition of the upper urinary tract appeared to influence the 5-year survivorship in patients with advanced prostatic carcinoma It was shown (table 1) that in patients without bone metastases, having at the time of treatment unilateral or bilateral hydronephrosis, the 5-year survivorship was 32 4 per cent, whereas in patients with normal upper urinary tracts the 5-year survivorship was 54 3 per cent provided treatment was by bilateral orchiectomy[6] followed by stilbestrol, usually 5 mg daily, and transurethral resection when indicated for the relief of bladder neck obstruction, and also provided that the patients survived unassociated disease The poor prognostic significance of the obstructed upper urinary tract can be further demonstrated in a study of 10-year survivorship in a series of 64 patients with advanced prostatic carcinoma followed 10 years or longer subsequent to bilateral orchiectomy and stilbestrol[7] In this series

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[1] Herbut, P A Urological Pathology Philadelphia Lea & Febiger, 1952, vol 2, p 947

[2] Graves, R C and Militzer, R E Carcinoma of the prostate with metastases J Urol , **33** 235, 1935

[3] Mintz, E R and Smith, G G Autopsy findings in 100 cases of prostatic cancer New Eng J Med , **211** 279–287, 1934

[4] Nesbit, R M and Baum, W C Endocrine control of prostatic carcinoma J A M A , **143** 1317–1320, 1950

[5] Ganem, E J Carcinoma of the prostate gland Five year survival following anti androgenic treatment J Urol , **74** 804, 1955

[6] Huggins, C , Stevens, R E Jr and Hodges, C V Studies on prostatic cancer The effects of castration on advanced carcinoma of the prostate gland Arch Surg , *43* 209, 1941

[7] Ganem, E J Advanced prostatic carcinoma A study of ten-year survival after anti-androgenic treatment New Eng J Med **254** 1086, 1956

TABLE 1 *Influence of hydronephrosis on 5 year survival 119 patients without bone metastases*

With Hydronephrosis (37 patients)	Without Hydronephrosis (82 patients)
2 died of unassociated disease	10 died of unassociated disease
12 survived 5 or more years	38 survived 5 or more years
5 year survival 32 4%	5 year survival 54 3%

TABLE 2 *Incidence of upper urinary tract disease 221 patients*

Normal upper tracts		148 patients (67%)
Hydronephrosis & hydroureter, unilateral or bilateral		67 patients (30 3%)
Miscellaneous pathological changes as follows		6 patients (2%)
Solitary serous cysts of kidney	2 patients	
Bilateral nephrolithiasis without hydronephrosis	1 patient	
Atrophic pyelonephritis	2 patients	
Left renal hypoplasia	1 patient	

not a single patient having hydronephrosis at the time of treatment survived 10 years

While it was initially hoped that information could be gained regarding the sole influence of orchiectomy and stilbestrol therapy on the upper tracts it became obvious that there were not enough patients in the entire series who were treated by these anti-androgenic measures alone to allow satisfactory analysis, as it appeared that most of these patients had some degree of bladder neck obstruction requiring surgical relief Thus it was decided that the net effects of both anti-androgenic treatment and transurethral resection would be evaluated rather than those of anti-androgenic treatment alone

The clinical records of 247 patients treated on the urological service of the Massachusetts General Hospital were reviewed In each instance the carcinoma was too extensive locally to allow serious consideration that complete extirpation by radical prostatectomy[5] might be possible

In 84 per cent of these patients the diagnosis was confirmed by histologic examination of tissue removed by transurethral resection or perineal biopsy with a Silverman needle In the remaining 16 per cent without histologic confirmation, the clinical examination and subsequent course of the patient left no reasonable doubt regarding the nature of the disease process present

Sufficient roentgenographic studies to allow satisfactory analysis were obtained in 221 patients In the vast majority the upper tracts were studied by intravenous pyelography but in a few retrograde pyelograms were obtained

It was found (table 2) that 148 patients or 67 per cent of the entire series had upper urinary tracts that were interpreted as being within normal limits Sixty-seven patients or 30 5 per cent had demonstrable unilateral or bilateral hydronephrosis and 6 patients or 2 7 per cent had miscellaneous pathological changes as follows

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[5] Young H H The cure of cancer of the prostate by radical perineal prostatectomy (prostato seminal vesiculectomy) History literature and statistics of Young s operation J Urol 53 188 1945

Two had solitary serous cysts of the kidney.

Two had chronic pyelonephritis without hydronephrosis or hydroureter.

One had bilateral nephrolithiasis without hydronephrosis or hydroureter.

One had an hypoplastic left kidney.

Thus one-third of all the patients with advanced prostatic carcinoma were shown to harbor upper urinary tract disease when first seen and in 92 per cent of these the lesion was unilateral or bilateral hydronephrosis.

Attention was then directed to the relative incidence of hydronephrosis in 2 separate groups of patients, namely, those with demonstrable bone metastases and those free of demonstrable bone metastases when first seen (table 3).

Among 57 patients with proven bone metastases there were 17 or 29.8 per cent who showed unilateral or bilateral hydronephrosis.

Among 164 patients without demonstrable bone metastases, hydronephrosis, either unilateral or bilateral, was present in 50 patients, an incidence of 30.4 per cent, a figure not far removed from that for patients with bone metastases.

In further analyzing these groups, it was found that among patients with metastases, the degree of obstruction was not significantly greater than among patients without metastases. Thus the hydronephrosis was bilateral in 57 per cent and unilateral in 43 per cent among patients with bone metastases. It was bilateral in 54 per cent and unilateral in 46 per cent in patients without bone metastases.

In both groups, slightly over half of the patients with upper tract obstruction had bilateral hydronephrosis.

Attention was then directed to the question of the fate of the obstructed upper urinary tract in patients with advanced prostatic carcinoma following anti-androgenic treatment (bilateral orchiectomy followed by stilbestrol 5 mg daily) and transurethral resection when indicated for the relief of bladder neck obstruction.

Sufficient data with followup pyelographic studies were available for analysis in the records of 33 patients. It is to be noted that all but 1 patient had transurethral resection for bladder neck obstruction, in addition to bilateral orchiectomy, and estrogenic hormones.

It was found that 4 possibilities existed.

1) Hydronephrosis could develop in a previously normal upper tract following anti-androgenic treatment and transurethral resection.

2) A normal tract could remain normal following treatment.

TABLE 3. *Incidence of hydronephrosis 221 patients*

With Bone Metastases (57 patients)	Without Bone Metastases (164 patients)
29.8% (17 patients)	30.4% (50 patients)
Bilateral in 57% Unilateral in 43%	Bilateral in 54% Unilateral in 46%

TABLE 4 *Fate of hydronephrosis following anti androgenic treatment and transurethral resection when indicated 33 patients*

16 patients	a	Normal	→ deteriorate →	Hydronephrosis
5 patients	b	Normal	→ remain →	Normal
4 patients	c	Hydronephrosis	→ {unchanged or deteriorate} →	More hydronephrosis
8 patients	d	Hydronephrosis	→ improve →	Less hydronephrosis or return to normal

60% deteriorated
40% remained the same, improved or showed complete return to normal

TABLE 5 *Progressive development of bone metastases following anti androgenic treatment in patients with hydronephrosis 28 patients*

Patients with Progressive Deterioration of Upper Tracts following Anti androgenic Treatment and Transurethral Resection	Patients with Improvement of Upper Tracts following Anti androgenic Treatment and Transurethral Resection
Bone metastases developed in 61%	Bone metastases developed in 16%

3) Unilateral or bilateral hydronephrosis before treatment could remain the same or increase in degree following treatment

4) Unilateral or bilateral hydronephrosis before treatment could improve or even show a complete return to normal following treatment

It was found among (table 4) these 33 patients that

1) Sixteen patients had normal upper tracts in which obstruction developed following treatment In 8 of these, the deterioration occurred within 2 years of treatment, and in 8 from 4 to 10 years following treatment

2) Five patients had normal upper tracts which remained normal following treatment for periods ranging from 6 months to 9½ years following treatment

3) In 4 patients who had hydronephrosis before treatment, the hydronephrosis increased following treatment, all within a 2-year period from the time of treatment

4) Eight patients who had hydronephrosis before treatment improved remarkably or had normal upper urinary tracts following treatment 2 within 5 months of treatment, 6 between 2 and 5 years after treatment

In brief, in 60 per cent the upper tracts deteriorated and in 40 per cent they remained the same, improved, or returned completely to normal following treatment

Attention finally was directed to a study of the fate of the upper tracts in relation to the subsequent development of bone metastases A series of 28 patients, all without demonstrable bone metastases when first seen and all treated by bilateral orchiectomy, stilbestrol, and transurethral resection, was investigated Of the patients showing increasing hydronephrosis 61 per cent also acquired bone metastases In the group of cases in which the upper tract improved, bone metastases were seen to develop in only 16 per cent

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8 patients	d	Hydronephrosis	→	improve	→	Less hydronephrosis or return to normal

60% deteriorated
40% remained the same, improved or showed complete return to normal

TABLE 5 *Progressive development of bone metastases following anti androgenic treatment in patients with hydronephrosis 28 patients*

Patients with Progressive Deterioration of Upper Tracts following Anti androgenic Treatment and Transurethral Resection	Patients with Improvement of Upper Tracts following Anti androgenic Treatment and Transurethral Resection
Bone metastases developed in 61%	Bone metastases developed in 16%

3) Unilateral or bilateral hydronephrosis before treatment could remain the same or increase in degree following treatment

4) Unilateral or bilateral hydronephrosis before treatment could improve or even show a complete return to normal following treatment

It was found among (table 4) these 33 patients that

1) Sixteen patients had normal upper tracts in which obstruction developed following treatment In 8 of these, the deterioration occurred within 2 years of treatment, and in 8 from 4 to 10 years following treatment

2) Five patients had normal upper tracts which remained normal following treatment for periods ranging from 6 months to 9½ years following treatment

3) In 4 patients who had hydronephrosis before treatment, the hydronephrosis increased following treatment, all within a 2-year period from the time of treatment

4) Eight patients who had hydronephrosis before treatment improved remarkably or had normal upper urinary tracts following treatment, 2 within 5 months of treatment, 6 between 2 and 5 years after treatment

In brief, in 60 per cent the upper tracts deteriorated and in 40 per cent they remained the same, improved, or returned completely to normal following treatment

Attention finally was directed to a study of the fate of the upper tracts in relation to the subsequent development of bone metastases A series of 28 patients, all without demonstrable bone metastases when first seen and all treated by bilateral orchiectomy, stilbestrol, and transurethral resection, was investigated Of the patients showing increasing hydronephrosis 61 per cent also acquired bone metastases In the group of cases in which the upper tract improved, bone metastases were seen to develop in only 16 per cent

SUMMARY AND CONCLUSIONS

The results of a clinical investigation of the upper urinary tracts in 221 patients harboring advanced prostatic carcinoma too extensive to allow complete extirpation by radical prostatectomy are reported

It is shown that one-third of all patients have upper urinary tract disease, nine-tenths of these had unilateral or bilateral hydronephrosis when first seen

The incidence and degree of unilateral and bilateral hydronephrosis are not significantly greater in patients with bone metastases than in those without bone metastases

Following anti-androgenic treatment and transurethral resection when performed for relief of bladder neck obstruction, it is found that in 60 per cent of patients the upper urinary tract will undergo progressive deterioration usually within 2 years of treatment in the direction of increasing hydronephrosis, while in 40 per cent the upper tracts will remain unchanged, or show either significant improvement or even complete return to normal

Progressive deterioration of the upper tracts following anti-androgenic treatment combined with surgical relief of bladder neck obstruction is a poor prognostic sign and appears to promise a much higher incidence of subsequent bone metastases than progressive improvement of the upper urinary tracts following the same treatment

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THE OCCURRENCE OF INTRAVENOUSLY INJECTED RADIOACTIVE ZINC IN THE PROSTATE AND PROSTATIC FLUID OF DOGS

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Zinc in the prostate was first found and measured by Bertrand and Vladesco[1] in 1921. Zinc also exists in appreciable concentrations as a trace element in the liver, pancreas, muscle and both red and white blood cells, and is present to a lesser extent in the spleen, brain, kidney and lung.[2] It has been demonstrated to be intimately associated with carbonic anhydrase[3] and exists in combination with protein in white blood cells.[4]

In rats, dietary zinc deficiency is known to produce hyperkeratinization, alopecia, manition and death[5] while excess dietary zinc is known to produce anemia and retardation in maturation.[6]

Mawson and Fischer showed that the prostate contains a higher concentration of zinc than any other soft tissue in the human.[7] They demonstrated that the concentrations of zinc in normal prostatic tissue and in benign hypertrophy are about equal but that carcinoma of the prostate and prostatic infection are associated with decreased concentrations of zinc. It has further been shown in the rat and rabbit that the presence of zinc in the prostate cannot be entirely accounted for by the presence of carbonic anhydrase or of red blood cells in the prostate.[8] Gunn and Gould have demonstrated a difference in the concentrations of radioactive zinc between the lateral and dorsal prostate of the rat and that concentrations of radioactive zinc in the dorsolateral prostate of the rat alter

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The co-operation of the Division of Clinical Investigation of Sloan Kettering Institute in general and of Dr. Martin Sonenberg in particular during the pursuit of these studies is gratefully acknowledged.

* Ruth Newman Van Horn Special Fellow in Surgery (Urology) July 1, 1954–June 30, 1955. Dr. Prout was awarded first prize for his presentation of this work in the annual essay contest sponsored by the New York Section of the American Urological Association, April 25, 1956.

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Progressive deterioration of the upper tracts following anti-androgenic treatment combined with surgical relief of bladder neck obstruction is a poor prognostic sign and appears to promise a much higher incidence of subsequent bone metastases than progressive improvement of the upper urinary tracts following the same treatment

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Tissues obtained by biopsy were placed in pre-weighed counting vials and reweighed immediately Each vial with its contents was then frozen Radioactivity was subsequently determined The per cent of the injected dose in each sample was expressed as radioactivity per gram of wet tissue (× 10^3) The organ/blood ratios were computed from these values, assuming blood to have a specific gravity of 1 0

EXPERIMENTAL

Exp 1 Dog X75 weighed 44 pounds preoperatively During the first three postoperative months, he lost five pounds Although his coat appeared quite poor at times, his activity and appetite always remained good Eight days postoperatively, he was given 1 ml of zinc chloride containing 80 microcuries of radioactive

TABLE 1 *Dog X75, given 1 ml of $Zn^{65}Cl_2$ containing 80 microcuries*

Days After Injection	Radioactivity in Dog Prostatic Fluid			Volume (ml) of Dog Prostatic Fluid		
	I	II	III	I	II	III
1	14 4	16 7	14 7	records lost		
5	samples lost			5 0	4 5	4 0
6	24 1	16 8	lost	13 0	II & III = 11 5 total	
12	30 9	15 2	15 2	lost	II & III = 10 8 total	
19	16 9	11 0	9 2	7 0	5 0	6 5
25	11 7	8 2	7 5	6 7	6 0	5 0
29	8 8	6 3	6 0	5 0	4 5	5 0
34	10 7	5 8	4 7	5 5	5 0	5 0
36	6 2	5 2	4 6	4 5	4 0	3 5
39	6 8	4 8	4 3	4 7	4 5	4 2
47	6 2	3 3	3 9	4 0	3 0	4 0
53	4 4	2 7	2 4*	3 0	4 0	3 5
61	4 2	2 1*	2 2*	5 5	4 0	4 0
70	4 2	2 7*	2 7*	4 0	4 0	3 7
77	2 9	lost	2 3	6 7	2 0	4 0
84	3 6	—	—	8 0	not collected	
89	3 8	—	—	6 5	not collected	
99	3 7	—	—	6 0	not collected	
106	3 9	lost	—	8 0	6 0	not collected
113	2 8	lost	—	7 0	5 5	not collected
120†	1 8	1 0	—	18 0	16 0	not collected
132	2 1	1 3	—	10 0	6 0	not collected
140	2 3	—	—	4 5	5 5	not collected
148	2 6	1 4	—	7 5	7 5	not collected

	Radioactivity in Whole Blood
1	3 0
5	2 7
7	2 5
12	1 7*

* Unsatisfactory counting rate

† Received 5 mg pilocarpine subcutaneously in addition to usual dose

under various endocrine influences[9, 10] Using a complex-forming buffer with dithizone, Mager, and others demonstrated histologically that zinc is found in the epithelial cells of the prostatic acini[11] Daniel, and others found significant amounts of radioactivity in the prostates of men after the intravenous injection of radioactive zinc and obtained radioautographs revealing radioactivity in the prostatic epithelium[1]

METHODS AND MATERIAL

Prostatic fistulas were created in healthy mongrels by the technique of Huggins[13] After the animals had recovered from the procedure, they were subjected to periodic prostatic stimulation Recovery was judged by the general behavior, appetite and stabilization of weight Prostatic stimulation was accomplished by giving a standard dose of 5 mg pilocarpine sulfate (1 mg /ml) intravenously at time zero

The prostatic fluid was collected in 100 ml graduated cylinders The volume was estimated from the cylinder and the fluid volumetrically transferred to 5 ml counting vials Prostatic fluid was collected in either two or three time-determined aliquots That fluid designated as DPI I was collected from time zero to 15 minutes, DPI II was collected from 15 to 30 minutes, and DPI III was collected from 30 to 60 minutes The last aliquot was omitted from the protocol after the first experiment

The radioactive isotope of zinc, Zn^{65}, was obtained as zinc chloride The carrier content was less than 300 mcgm zinc in every experiment The isotope was administered intravenously in every instance

The radioactivity in the samples obtained was determined in a well-type scintillation counter Volumes of one or two ml of dog prostatic fluid were counted If low activity was anticipated, three or four ml were employed, but this was done rarely Appropriate corrections for background were made A standard dilution of the radioactive zinc injected was made each time an experiment was commenced and was counted with samples each time these were obtained

The radioactivity recovered in 1 ml of dog prostatic fluid was expressed as a percentage of the total radioactivity administered This value is expressed as 10^3 in the accompanying charts and figures and is henceforth referred to as radioactivity in dog prostatic fluid

Blood was obtained by venipuncture before the injection of pilocarpine and its radioactivity similarly determined and expressed

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Days After Injection	Radioactivity in Dog Prostatic Fluid			Volume (ml.) of Dog Prostatic Fluid		
	I	II	III	I	II	III
1	14.4	16.7	14.7	records lost		
5	samples lost			5.0	4.5	4.0
6	24.1	16.8	lost	13.0	II & III = 11.5 total	
12	30.9	15.2	15.2	lost	II & III = 10.8 total	
19	16.9	11.0	9.2	7.0	5.0	6.5
25	11.7	8.2	7.5	6.7	6.0	5.0
29	8.8	6.3	6.0	5.0	4.5	5.0
34	10.7	5.8	4.7	5.5	5.0	5.0
36	6.2	5.2	4.6	4.5	4.0	3.5
39	6.8	4.8	4.3	4.7	4.5	4.2
47	6.2	3.3	3.9	4.0	3.0	4.0
53	4.4	2.7	2.4*	3.0	4.0	3.5
61	4.2	2.1*	2.2*	5.5	4.0	4.0
70	4.2	2.7*	2.7*	4.0	4.0	3.7
77	2.9	lost	2.3	6.7	2.0	4.0
84	3.6	—	—	8.0	not collected	
89	3.8	—	—	6.5	not collected	
99	3.7	—	—	6.0	not collected	
106	3.9	lost	—	8.0	6.0	not collected
113	2.8	lost	—	7.0	5.5	not collected
120†	1.8	1.0	—	18.0	16.0	not collected
132	2.1	1.3	—	10.0	6.0	not collected
140	2.3	—	—	4.5	5.5	not collected
148	2.6	1.4	—	7.5	7.5	not collected
	Radioactivity in Whole Blood					
1	3.0					
5	2.7					
7	2.5					
12	1.7*					

* Unsatisfactory counting rate.

† Received 5 mg. pilocarpine subcutaneously in addition to usual dose.

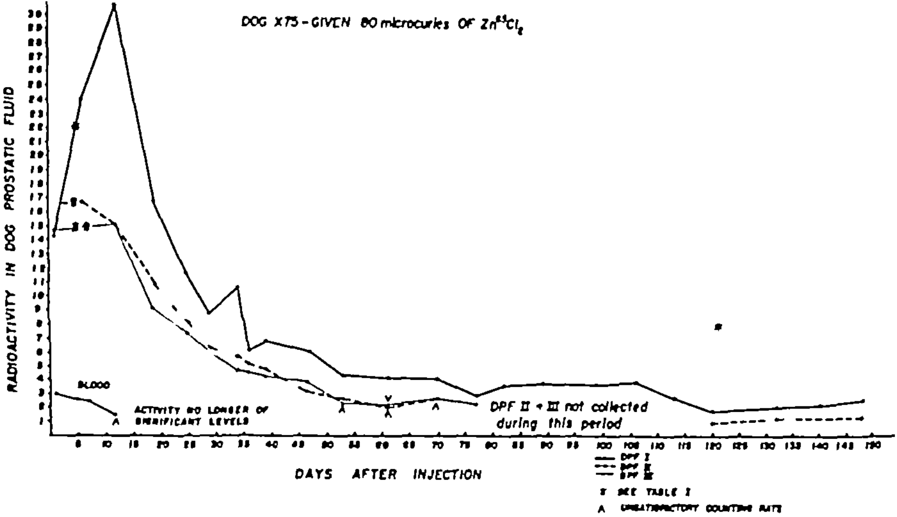

Fig 1

Table 2 *Dog X75, given 1 ml of $Zn^{65}Cl$ containing 66 microcuries Estradiol 12 5 mcgm intramuscularly started on 12th day after injection of Zn^{65} and stopped on 34th day*

Days Before Injection	Radioactivity in Dog Prostatic Fluid		Volume (ml) of Dog Prostatic Fluid	
	I	II	I	II
13			8 0	not collected
7			6 5	8 0
2			8 0	3 0
Days After Injection				
1	29 9	17 1	6 0	5 0
3	25 9	17 6	8 0	4 5
6	34 0	19 9	10 0	5 0
8	20 0	15 4	8 0*	4 0
11	24 3	11 5	9 0	5 0
14	15 7	9 8	8 0	5 0
18	11 4	9 1	5 0	2 0
21	9 3	7 0	4 0	2 0
25	—	—	0 0	0 0
29	I & II combined = 3 0		1 ml in 30 minutes	
35	I & II combined = 3 8		1 ml in 30 minutes	
39	7 2	not counted	1 5	75
43	lost	lost	4 0	3 5
47	4 7	2 7	10 0	2 0
50	4 5	2 4	9 0	2 0
53	3 6	lost	6 0	4 5
57	3 3	2 8	7 0	3 5
60	4 3	2 9	not recorded	
63	3 8	2 7	9 0	4 0
67	2 8	2 3	7 0	6 0
69	lost	1 3	1 0	4 0
75	3 4	3 4	5 0	4 0
79	4 0	2 4	7 0	6 0
83	4 0	2 4	6 5	5 0
86	3 2	2 1	8 0	5 0
89	2 6	2 2	4 0	4 0
93	3 5	2 3	6 5	4 0
97	2 2	1 8	11 0	6 5

* First part lost

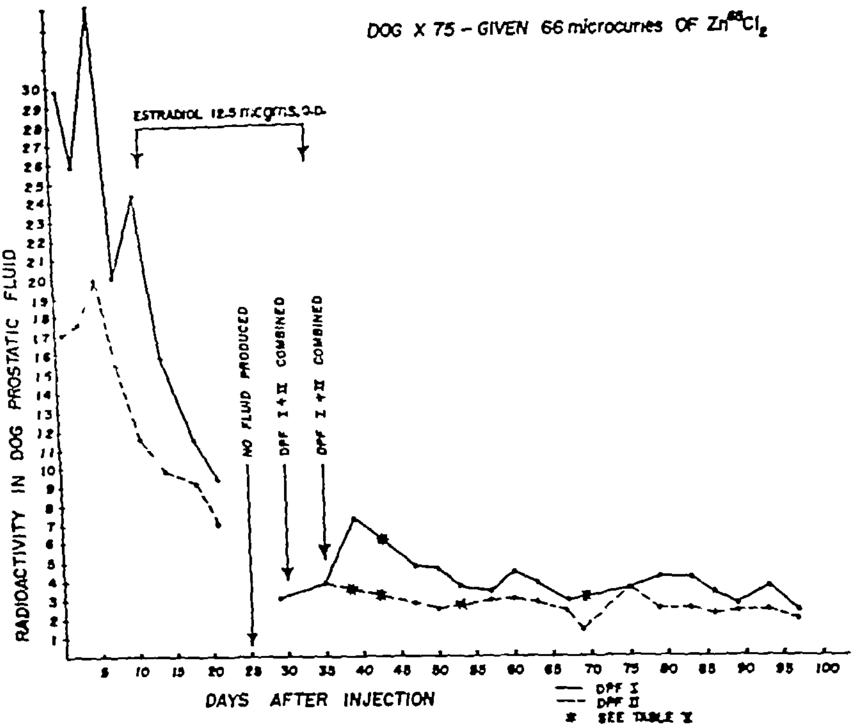

FIG 2

zinc, and prostatic fluid was obtained at varying intervals, thereafter The results are shown in table 1 and figure 1

Exp 2 After radioactivity in the prostatic fluid of X75 had dropped to insignificant levels and nine months had passed since the initial injection of radioactive material a second injection of 1 ml of zinc chloride containing 66 microcuries of radioactive zinc was given On the twelfth day, thereafter, 12 5 mcgm of estradiol* intramuscularly daily was begun and continued through the thirty-fourth day Prostatic fluid was obtained at varying intervals, thereafter The results are shown in table 2 and figure 2

Exp 3 One hundred and thirteen days after the second injection of radioactive zinc X75 was given a third dose of 2 ml of zinc chloride containing 125 microcuries of radioactive zinc Estradiol (12 5 mcgm) intramuscularly daily for 12 days was simultaneously initiated Prostatic fluid was obtained at varying intervals, thereafter The results are shown in table 3 and figure 3

Exp 4 Dog X42 experienced wound dehiscence following preparation of the fistula and the animal lost 14 pounds in the ensuing six weeks Subsequently, his weight stabilized and coat improved Eight weeks after preparation, he was given 1 6 ml zinc chloride containg 60 microcuries of radioactive zinc Prostatic fluid was obtained at varying intervals, thereafter The results are shown in table 4 and figure 4

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* Progynon aqueous suspension, produced by Schering Corporation Bloomfield N J

TABLE 3 *Dog X75, given 2 ml of $Zn^{65}Cl_2$ containing 125 microcuries Estradiol, 12.5 mcgm intramuscularly, was given on day zero and on each day thereafter until 12th day*

Days Before Injection	Radioactivity in Dog Prostatic Fluid		Volume (ml) of Dog Prostatic Fluid	
	I	II	I	II
8	2.2	1.8	11.0	6.5
4	—	—	13.0	3.5
1	2.5	1.5	12.0	3.0
Days After Injection				
1	19.7	16.1	6.5	5.0
4	30.1	17.0	12.0	5.0
5	21.7	13.2	3.0	2.0
8	not counted		0.5	1.0
11	I & II combined = 9.0		0.5	1.5
13	3.0	not counted	1.0	0.5

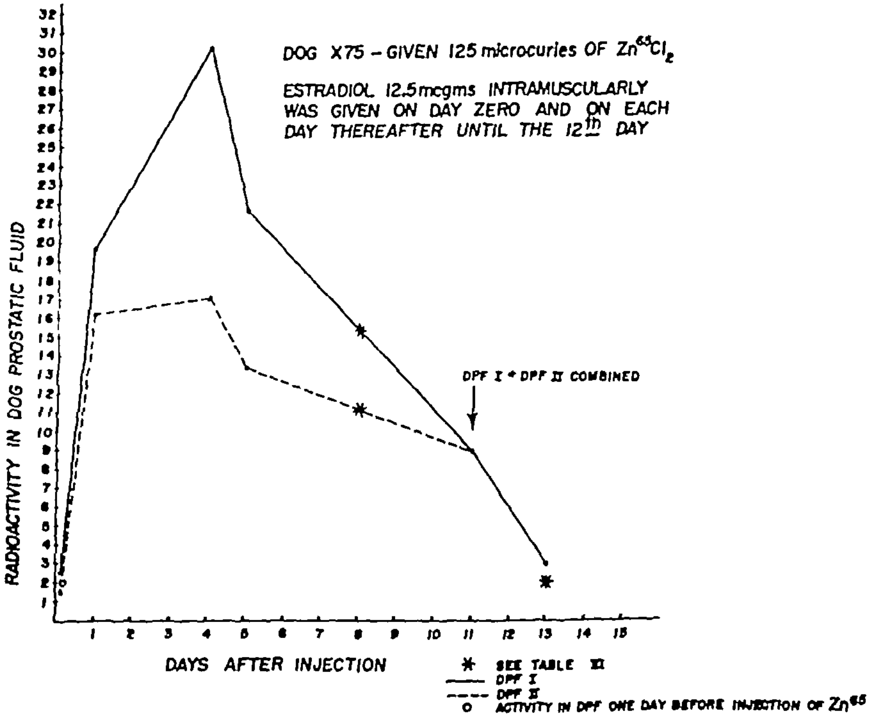

FIG 3

Exp 5 Dog X66 had a benign postoperative course following preparation of the prostatic fistula but did not regain his preoperative weight and vigor until several months after preparation Five months after operation, he was given 1 ml of zinc chloride containing 66 microcuries of radioactive zinc Prostatic fluid was obtained at varying intervals, thereafter The results are shown in table 5 and figure 5

TABLE 4 *Dog X42, given 1.6 ml of $Zn^{65}Cl$ containing 60 microcuries*

Days Before Injection	Radioactivity in Dog Prostatic Fluid		Volume (ml.) of Dog Prostatic Fluid	
	I	II	I	II
22			7.0	8.5
18			8.0	7.0
9			5.5	3.5
Days After Injection				
1	13.0	10.3	3.0	3.0
4	—	14.3*	0.0	records lost
9	—	14.6*	0.0	5.0
13	11.2	11.1	2.5	5.0
17	9.6	8.2	2.0	3.0
23	7.8	8.6	0.7	5.0
25	5.5	5.3	2.0	2.0
29	5.7	6.2	2.5	7.0
33	4.1	4.2	1.0	4.0
37	4.1	4.0	2.0	4.0
39	—	3.4*	0.0	1.0
42	3.2	2.7	2.0	4.0
44	—	2.9*	0.5	3.0
50	4.1	2.7	5.0	3.5
54	4.0	2.9	records lost	
57	3.5	2.4	6.5	2.5
61	3.4	2.5	3.0	3.0
65	1.5	0.8†	6.5	4.5
71	3.3	2.1	5.0	4.0
75	3.2	2.5	5.0	4.0
79	3.4	2.7	5.0	1.0 (part lost)
86	3.0	3.0	5.5	4.0
89	4.3	2.4	2.0	2.0
93	3.3	not counted	6.0	6.0
96	3.0	not counted	2.0	3.0
99	3.7	2.5	6.5	2.0
103	not counted	2.2	6.5	3.5
105	2.4	2.3†	1.0	4.0
111	2.2	1.6†	4.0	2.0
115	2.1	1.1	6.0	3.0
122	3.0	1.6	lost	2.3

* These values are shown in figure 4 as DPF I

† Unsatisfactory counting rate

Exp 6 Dog X4 had no prior operation but was injected intravenously with 1.8 ml of zinc chloride containing 100 microcuries of radioactive zinc. Seven days later, under intravenous pentothal anesthesia, biopsies were obtained from the liver, pancreas, prostate, testis and epididymis. Venous blood specimens were obtained at this time. The animal expired at the end of the procedure for no apparent cause. Data concerning radioactivity in these biopsies are shown in table 6 and figure 6.

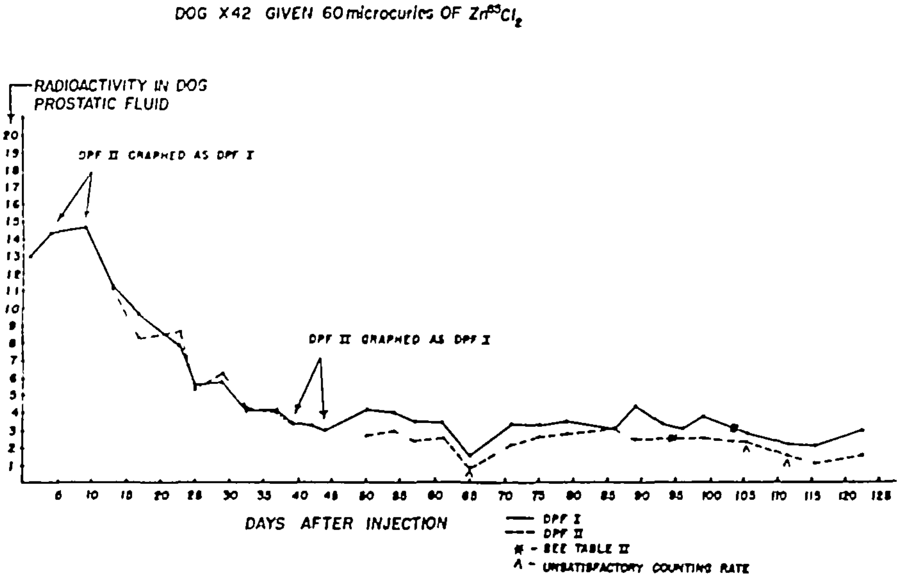

FIG 4

TABLE 5 *Dog X66, given 1 ml of $Zn^{65}Cl$ containing 66 microcuries*

Days Before Injection	Radioactivity in Dog Prostatic Fluid		Volume (ml) of Dog Prostatic Fluid	
	I	II	I	II
23			2.0	5.0
13			1.0	5.0
Days After Injection				
1	19.5	13.3	3.5	3.5
4	—	16.4*	0.0	4.0
8	22.7	17.4	2.0	3.0
11	11.6	13.4	1.5	5.0
14	I & II combined = 14.1*		0.5	1.0
18	11.6	7.3	records lost	
21	9.1	not counted	2.0	1.0
25	5.8	3.7	3.5	5.0
29	6.1	3.3	6.5	2.5
35	4.7	2.8	6.0	2.0
39	3.7	3.7	2.0	1.0
45	3.3	2.4	2.0	2.0
50	4.4	2.9	6.0	5.0
53	3.8	not counted	6.0	5.0
58	3.7	2.5	5.0	3.0
61	3.1	1.8†	6.0	2.5
64	3.0	2.1†	5.0	3.0
68	2.4	2.1	4.0	2.5
72	1.9	1.7	3.5	3.5
78	2.6	2.1	3.0	4.0
83	2.5	1.3†	7.0	1.5
86	2.5	2.1	2.5	3.5
89	—	1.3†	lost	5.0
92	2.3	1.3	6.5	4.0
96	2.2	1.6	6.5	4.0
99	2.4	not counted	9.5	5.5

* These values are shown in figure 5 as DPF I

† Unsatisfactory counting rate

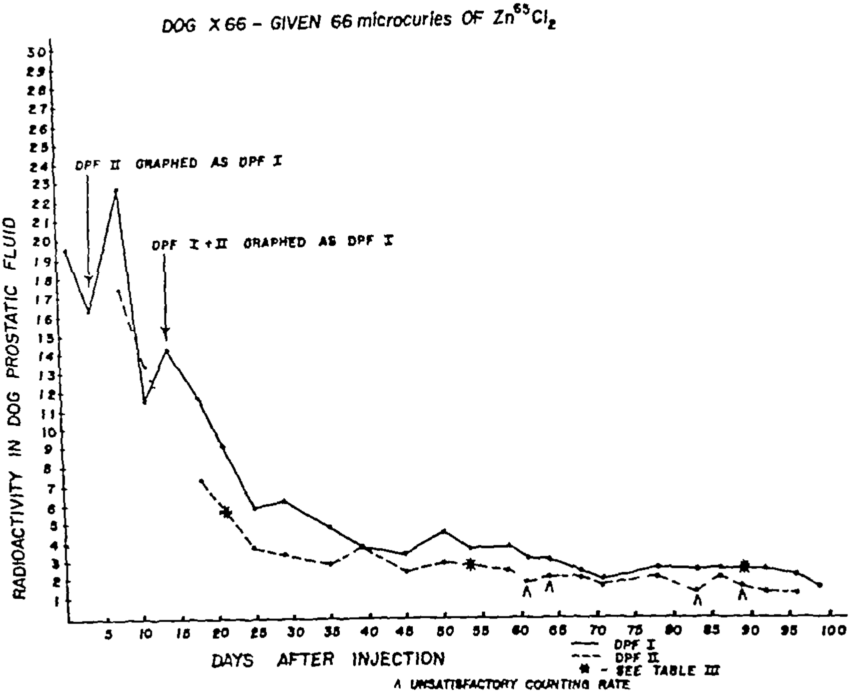

FIG 5

None of the animals demonstrated any grossly detectable deleterious effects after the injections of the zinc

RESULTS

When the dogs with prostatic fistulas were given intravenous radioactive zinc and stimulated with a standard dose of intravenous pilocarpine, the resultant prostatic fluid always contained portions of the injected radioactivity

Radioactive zinc was detected in the prostatic fluid of the three control animals, X75, X42, and X66, for 147 days, 122 days and 99 days, respectively X75 was given pilocarpine 24 times, X42, 31 times, and X66, 26 times Radioactive zinc was present whenever prostatic fluid was produced during these periods

Radioactivity in blood fell rapidly to a level where the counting rate was too close to background to be significant (table 1, fig 1)

The volume of prostatic fluid collected at standard intervals showed inconstant, unpredictable variations from dog to dog and even in the same animal

The curves of the concentrations of radioactivity in the prostatic fluid in the three control experiments are similar in that a peak of concentration of radioactivity was reached within four to twelve days after the injection of $Zn^{65}Cl_2$ (exp 1, 4 and 5, figs 1, 4 and 5) A similar peak of radioactivity was reached when X75 received a second injection of radioactive zinc before estradiol was given (exp 2, table 2, fig 2) The concentration of radioactivity gradually

Table 6. *Dog X4, given 1.8 ml. of $Zn^{65}Cl_2$ containing 100 microcuries*

Tissue	Wet Weight (mg.)	N C/M/Gm	Radioactivity Per Gram of Wet Tissue	Organ/Blood
Prostate (left lobe)	291.7	54951	300	69
Pancreas	1050.6	4197	23	5.3
Right testis	1930.7	1939	11	2.4
Right epididymis caudal portion	284.3	2812	15	3.5
Right epididymis cephalic portion	366.2	2512	14	3.1
Liver	378.5	6969	38	8.7
Blood	2 ml	798	4	—
Plasma	2 ml	counting range too low to be significant		

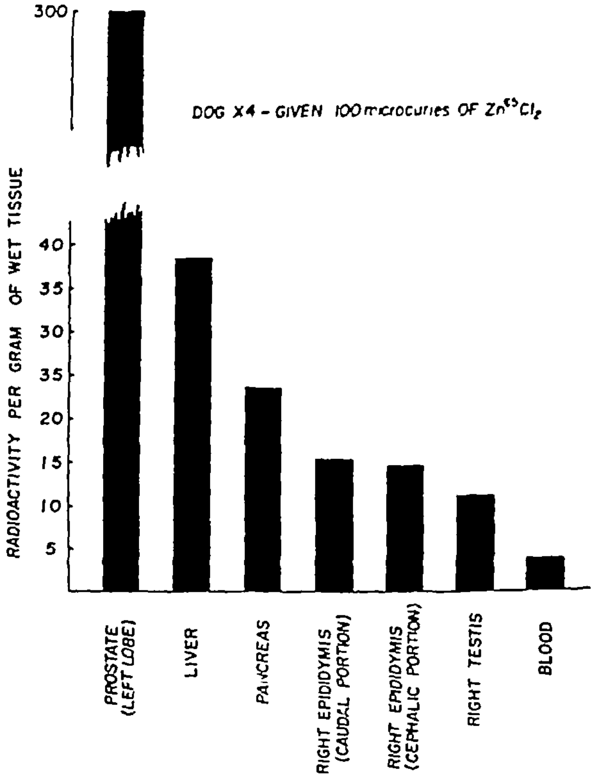

Fig. 6

decreased after the initial rise. The curve became asymptotic to the baseline after 35 to 53 days. In experiment 2 the concentration of radioactivity in DPF I and DPF II fell to a low of three seventeen days after the initiation of the first course of estradiol (table 2, fig. 2). When the second course of estradiol was started simultaneous with radioactive zinc administration, the concentration of radioactivity fell to three in DPF I in 13 days (exp. 3, table 3, fig. 3).

COMMENT

Graphical representation of the concentrations of radioactivity in dog prostatic fluid obtained under the conditions of these experiments indicated that the resultant curves followed a similar pattern The radioactivity in DPF I and DPF II (and in DPF III where shown) paralleled each other with a great degree of predictability, once the first two weeks had passed Prior to that time, the concentration of radioactivity in DPF I was relatively greater than in the other aliquots A peak of activity was seen on all of the curves although it varied slightly both in time and in amount from dog to dog and from experiment to experiment Only rarely was more radioactivity found in DPF II than in DPF I throughout the course of all the experiments

The curves also demonstrated that the radioactivity was highly predictable not only in terms of the relative radioactivity of DPF I and DPF II but also in terms of total recoverable radioactivity Furthermore, this highly predictable radioactivity persisted in prostatic fluid for at least three months in spite of many separate injections of intravenous pilocarpine during that period

Zinc occurs in relatively large amounts in prostatic fluid[14] and the relatively high concentrations of radioactive zinc found in the studies presented here are consistent with this fact From histochemical studies in the dog, monkey, rabbit, and man, it is known that zinc is present in the cells lining the prostatic acini [11] This has also been demonstrated by radioautographic techniques in man [12] It, therefore, seems probable that the zinc found in human prostatic fluid and the radioactive zinc in canine prostatic fluid arise from the same source, the prostatic epithelial cells of the respective species

It is of interest that the radioactivity in the dog prostatic fluid remains high for a three or four-week period after a solitary injection of radioactive zinc This suggests that either sufficient radioactive zinc is initially deposited in the prostatic epithelial cells to account for the relatively prolonged, high concentration, or the initial concentration in the cells is not so great but is supplemented with radioactive zinc from some as yet unidentified source

After the injection of radioactive zinc into an otherwise normal dog, the prostate was found to contain the greatest concentration of radioactivity of the organs biopsied Of the genital organs examined, the prostate was found to have the highest concentration of radioactivity at the time explored, manifesting thirty times the radioactivity of the testis and twenty times the radioactivity of the epididymis (table 6, fig 6) Measurements of total zinc in the human testis, and the testis and epididymis of the rat by Eggleton[2] were low when compared to other organs sampled and parallel our findings with radioactive zinc in the corresponding organs of the dog Yet Mawson and Fischer[14] demonstrated that human sperm contain much more zinc than the prostate and Mann[15] has made similar observations in the semen of the ram Numerous sperm counts done on

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[14] Mawson, C A and Fischer, M I Zinc and carbonic anhydrase in human semen Biochem J 55 696, 1953

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DPF during the course of our experiments usually demonstrated 1,000,000 ± 500,000 sperm/ml. but on many occasions no sperm were seen. Accordingly, it is evident that the radioactivity observed must have been derived almost completely from the prostatic fluid, rather than from the few sperm that may have been present. Possibly, much of the zinc found in mammalian sperm is actually derived from the prostatic fluid. Experiments to investigate this possibility are in progress.

Although the effect of estradiol was to reduce the volume of prostatic secretions, the effect on Zn^{65} was not so clear-cut. As long as prostatic fluid was produced, the isotope was present. During the first course of estradiol (exp. 2, table 2, fig. 2), the fall in the concentration of radioactivity as well as the total Zn^{65} output in the stated periods, was more rapid than that seen in the same animal under control conditions (exp. 1, table 1, fig. 1).

Under the influence of estradiol, the concentration of radioactivity found in the prostatic fluid reached a level of 3.0 in 29 days in experiment 2, while in experiment 1, the control study, it took 61 days for the concentration of radioactivity to drop to 4.2. When estradiol was initiated simultaneous with an injection of 125 microcuries of radioactive zinc in experiment 3 (table 3, fig. 3) the peak of radioactivity was seen in four days and only reached a level of 30.1, yet this was the largest amount of radioactive material given in any of the experiments. Thereafter, in experiment 3, the volume of prostatic fluid and concentration of radioactivity fell sharply, the concentration of radioactivity reaching 3.0 in 13 days. These findings suggest that estradiol directly or indirectly produced an effect on the prostate to decrease not only the volume of fluid but also the concentration of the isotope in the fluid produced.

From the data obtained in the experiments as outlined, it appears possible that the presence of zinc in dog prostatic fluid represents an integral function of the prostate.

SUMMARY

Using dogs prepared with prostatic fistulas, it has been demonstrated that the injected radioactive isotope of zinc, Zn^{65}, will appear in dog prostatic fluid in a highly predictable manner on repeated stimulation with pilocarpine sulfate.

Radioactivity was nearly always greater in the first portion of dog prostatic fluid collected than in the second.

Biopsy of various canine organs seven days after the injection of radioactive zinc revealed the radioactivity in the prostate to be much greater than that found in other tissues sampled.

In the few experiments performed, estradiol produced a rapid drop in volume and both concentration and total amount of radioactivity in dog prostatic fluid.

During the study periods, prostatic fluid was never obtained isotope-free, whether under the influence of estradiol or not.

From the above evidence, it would appear that the presence of zinc in the prostatic fluid of dogs is associated with an integral function of the canine prostate.

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PRELIMINARY EVALUATION OF RADIOACTIVE COLLOIDAL GOLD IN TREATMENT OF CARCINOMA OF THE PROSTATE

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From Brooke Army Hospital, Fort Sam Houston, Texas

In May 1952, Dr Rubin Flocks of the University of Iowa read a paper entitled "Treatment of Carcinoma of the Prostate With Radioactive Gold (AU-198)" at Brooke Army Hospital Stimulated by his work, Colonel C C Dodson, then chief of urology at Brooke Army Hospital, instituted a program of treating certain cases of carcinoma with AU-198, starting in July 1953 This program has been continued under the present chief of the service, Colonel L K Mantell, and at the present time 20 cases have been treated with radioactive gold

Radioactive colloidal AU-198, with particle sizes ranging from 0 003 to 0 004 micron, was used The isotope has a half life of 2 7 days and possesses suitable radiation characteristics It is made in a nuclear reactor by bombarding stable AU-197 with neutrons and it decays to a stable isotope of mercury, giving off gamma and beta radiation in the process It emits beta rays with maximum energy of 0 97 million electron volts and gamma rays of 0 411 million electron volts Fifty per cent of the beta rays penetrate 3 8 mm of tissue and are the source of the radiation effect in localized areas The gamma rays penetrate deeply and are useful in external counting, but they may also contribute to both local and total body radiation One millicurie decayed in one gram of tissue yields 0 76 equivalent roentgens

One milliliter of epinephrine hydrochloride (1–1,000) and 150 units of hyaluronidase are added to the isotope Isotonic saline was used to dilute the material to the proper volume

Patients selected for radioactive gold treatment fell in the group 2 classification of Dr Flocks, that is, the carcinoma had extended beyond the prostatic capsule although there was no evidence of distant metastasis Approximately 50 to 55 per cent of the patients seen with carcinoma of the prostate are in this group If the patient had obstructive symptoms, as four in our series had, a transurethral resection was done 3 to 4 weeks prior to injection of the radioactive gold By this means, the obstruction was alleviated and the tumor mass to be injected was reduced

The technique of injecting the gold is simple We use an intravesical approach through a lower abdominal midline incision A lead-walled syringe, similar to one used by Dr Flocks, which was modified by personnel at Brooke Army Hospital, is used The gold is injected in 12 areas around the bladder neck into the prostate and one area in each seminal vesicle We inject 2 5 to 3 *millicuries* per gram of prostatic tissue, with a maximum of 150 millicuries Using this dosage, with a concentration of 5 millicuries per cubic centimeter of solution, we have noted no rectal or prolonged bladder neck irritation In earlier cases drainage was

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Read at annual meeting of South Central Section of American Urological Association, Mexico City, October 28–November 1 1956

*Present address 1216 Pennsylvania Ave, Fort Worth 4 Texas accomplished with both a suprapubic catheter and an indwelling urethral catheter Recently we have dispensed with the suprapubic catheter and have noted an improvement in the patient's wound healing All initial injections are done suprapubically through cystotomy incision Followup injections, as indicated, are done transperineally

A few technical precautions should be mentioned Using film badges, we have found that the highest exposure recorded per individual is 40 milliroentgens, with the average exposure running between 25 and 30 milliroentgens Based on a total of 300 milliroentgens in a 48-hour week, this has not been deemed an excessive amount of radiation to the individual The most commonly contaminated pieces of equipment are the skin towels, drape sheet, sponges, suction equipment, and sponge forceps Rarely are the gowns or gloves contaminated The contaminated equipment is placed in a large metal bin in the basement and allowed to decay Since it takes 7 half lives to decay down to 1 per cent of the original strength, after two weeks these contaminated objects are entirely safe to handle and are returned to the operating room

Postoperatively, the patients are isolated in a private room We are fortunate in having an air-conditioned room adjoining the isotope section and our patients are left there for variable periods of time, depending upon the amount of gold they receive While patients are in this room, various studies can be conveniently made by the isotope section

It is our belief that this procedure presents no undue hazards to the operating personnel if reasonable care is exercised We have been using two teams—one to inject the gold and the other to close the wound—in an effort to cut down the time of exposure Due to the low amount of contamination, however, this is probably an unnecessary precaution

Routinely, patients are taken to the isotope unit 5 or 6 days postoperatively and are examined by means of a scintiscanner An example of the distribution of radioactive material 4 or 5 days following injection is shown in figure 1 Note the concentration of radioactivity in the area of the prostate

Since 1947, 85 patients with carcinoma of the prostate have been seen at Brooke Army Hospital Six of them received no treatment, as the diagnosis was

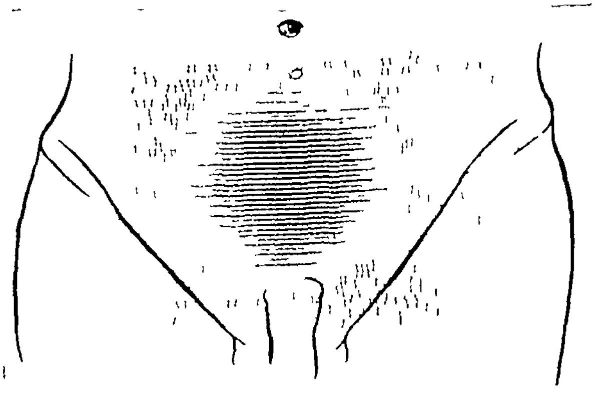

FIG 1

made at autopsy after the patient presented himself at the hospital with carcinomatosis Ten patients underwent curative perineal or radical retropubic prostatectomies Of these ten, eight are alive and well Only two have survived longer than five years and the survival rate since diagnosis is 2 4 years

Forty-nine were treated with orchiectomy, estrogens, and relief of obstruction either by suprapubic prostatectomy or transurethral resection The average survival period is 1 9 years

The remaining 20 patients received treatment with radioactive gold Of these 20, 16 are still alive Of 4 patients who died 3 died of widespread carcinoma arising from the prostate and one died of carcinoma of the pancreas These 4 patients died in the sixth twenty-first, thirty-fourth and thirty-fifth months following the initial injection Five patients have positive Silverman needle prostatic biopsies and have been re-treated by the perineal route 1 to 4 times The average survival period of the 20 cases is 22 months

Of the seven patients surviving more than two years after operation, 4 have positive Silverman needle biopsies despite numerous perineal injections and two of these have demonstrable bony metastasis We have only 3 of 9 patients sur-

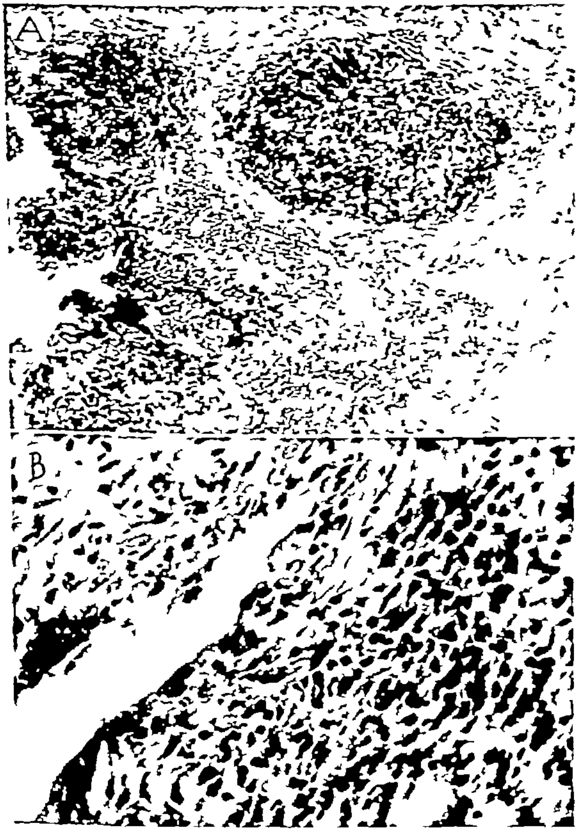

FIG 2

viving beyond the 1 8- to 2-year average time without treatment who are free of disease, according to x-ray or biopsy findings

Although no definite conclusions can be drawn from this small series, it is our feeling that there is merit to this treatment if the proper criteria for selection of cases are followed We have been impressed by the *immediate* improvement of the prostate on digital examination and postoperative negative Silverman needle biopsies Figure 2, A shows a preoperative lesion obtained by transurethral resection and figure 2, *B* shows a 3 months' postoperative Silverman needle biopsy revealing mild radiation effect Subjectively, the patients have shown improvement and apparently are more comfortable While the majority of patients are not cured, their disease may be controlled for varying lengths of time More time and patients are needed thoroughly to evaluate this treatment which may have some palliative, if not curative, effect

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ANORECTAL MALFORMATIONS AND ASSOCIATED URINARY FISTULAS: REPORT OF ONE HUNDRED CASES

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A great deal has been written about the problem of anorectal malformations, their embryology, incidence, and the methods of management, but little emphasis has been placed on the associated urinary fistulas and their *preoperative* diagnosis. To emphasize the need for preoperative urological workup to determine the presence or absence of a urinary fistula, the 100 cases of this anomaly seen at the St. Louis Children's Hospital between 1933 and 1956 have been reviewed. Many poor results could be attributed to the failure to recognize an intestinal-urinary fistula preoperatively. Seventeen patients had such fistulas which were unsuspected preoperatively but which could have been demonstrated if an adequate urological workup had been performed. A considerable number of these patients received initial surgical care at another institution and then came to this hospital for further corrective procedures.

The embryology of anorectal malformations and the associated urinary fistulas is twofold. Urinary fistulas are due to incomplete division of the cloaca, in the 3-week embryo, into the anterior bladder and the posterior primitive rectum by the urorectal septum. The different types of anorectal malformations are due to varying degrees of failure of the primitive rectum to join with the anus and its temporarily occlusive membrane.

Various classifications of these malformations have been proposed, and the one that is now generally used as the most practical working classification is that of Ladd and Gross,[1] although this is admittedly an oversimplification of the problem. The types described by these authors have been well illustrated by Santulli[2] and are shown in figure 1.

The occurrence of anorectal malformations varies according to different authors, the range being 1 in 800 to 1 in 10,000 births,[2, 3] the figure usually quoted being 1 in 5,000. The ratio between the sexes varies between equal male and female distribution to preponderance in the males. In this series, the distribution was 68 males to 32 females, a ratio of about 2:1.

The incidence of either intestinal or urinary fistulas cited in the literature varies between 30 per cent and 80 per cent;[2, 4-6] the incidence here was 60 per

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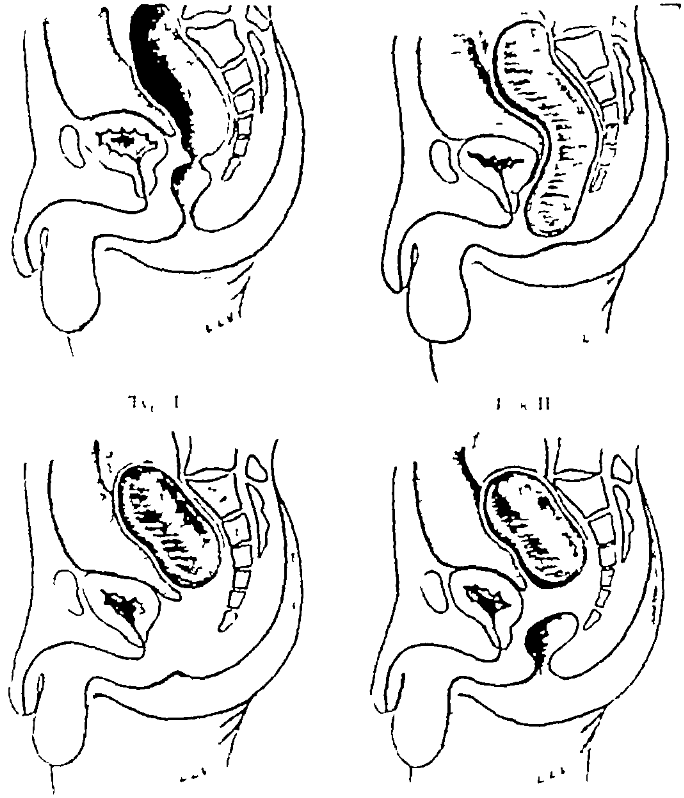

Fig I

Fig II

Fig III

Fig IV

FIG 1 From Santulli Surg, Gynec & Obst 95 601, 1952

cent Figure 2[2] illustrates these various fistulas and table 1 gives the percentage of their occurrence in this series

The various types of anorectal anomalies and the associated urinary fistulas are listed in table 2 The great preponderance of type 3 cases agrees with other series[2, 6, 7] The overall incidence of intestinal-urinary fistulas in our series was 29 per cent which agrees closely with that reported by others[6, 7, 8] Considering that all of the intestinal-urinary fistulas in our series occurred in males, this gives an incidence of these fistulas in the males of 42 per cent Seventeen of these, or over one-half, were not suspected preoperatively

The incidence of associated anomalies in our series is listed in table 3 Fifty-eight per cent of our patients had one or more additional anomalies, while other authors report an incidence varying between 22 per cent and 72 per cent[2, 7, 9, 11]

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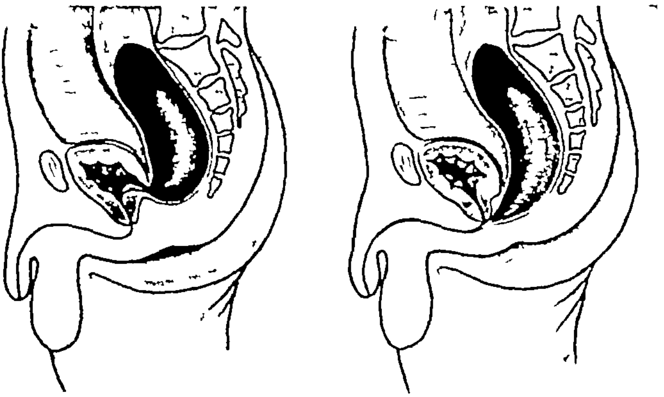
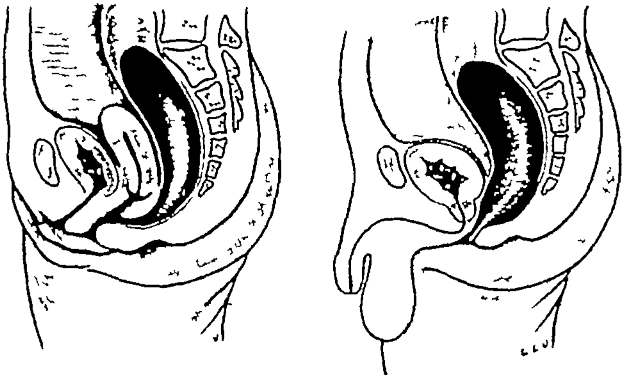


Rectovesical Rectourethral



Rectovaginal Rectoperineal

FIG 2 From Santulli Surg , Gynec & Obst , 95 601, 1952

The anomalies that were encountered are listed in table 4 Not including urinary fistulas, 32 per cent of these cases had one or more associated genitourinary anomalies

The routine method for diagnosing the type of anorectal malformation is the use of an x-ray of the infant taken in the inverted, or Wangensteen-Rice position,[1] using a metallic marker over the area where the anus should be An erroneous impression of the length of the defect between the "anus" and the rectum may be obtained if the above procedure is employed before the infant is 24 hours old as the intestinal gas may not have reached the most distal portion of the blind rectum

This procedure does not demonstrate the rectourinary fistulas, therefore, additional diagnostic studies are necessary Unfortunately, the method for demonstrating associated urinary fistulas, even if pursued, is far from standardized The most common site of an intestinal-urinary fistula is between the rectum and the prostatomembranous urethra The usually employed cystogram made by the instillation of a radiopaque medium through a catheter passed into the bladder

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TABLE 1 *Anorectal malformations and associated fistulas in 60 cases*

Type of Fistula	Number	Per Cent
Rectourethral	24	40
Rectovaginal	22	37
Rectoperineal	9	15
Rectovesical	5	8

TABLE 2 *Types of anorectal malformations and associated urinary fistulas*

Type of Malformation	Total Number	Number with Fistula	Per Cent
I	17	1	6
II	5	0	0
III	77	28	36
IV	1	0	0

TABLE 3 *Associated anomalies in 58 cases*

Type	Number	Per Cent
Genito renal	32	55
Gastrointestinal	16	28
Musculoskeletal	16	28
Cardiovascular	7	12
Miscellaneous	13	22

will rarely, if ever, demonstrate such a defect Our routine at present for demonstrating fistulas in the male involves taking a urethrocystogram using a watery solution of any appropriate radiopaque medium A viscous medium is not desirable, as it may not penetrate the small caliber fistulas The medium is injected with a suitable blunt-nosed syringe into the external urinary meatus and the x-ray picture taken while the injection is being made, lest the medium be squeezed out a tiny tract upon relaxation of the injection pressure Such an examination takes but a few minutes, entails no risk to the patient, and can yield much valuable information Renal function of the newborn is inadequate to permit satisfactory intravenous pyelographic evaluation of the upper urinary tract, so such thoroughness is beyond the limits of practicability

A thorough discussion of the best management of the primary anorectal malformation is beyond the scope of this presentation However, in order that the information obtained from this analysis might not be overlooked, the results of different methods of management of each type of deformity are listed in table 5 While all of these figures are small and therefore the difference of a few cases in any category would greatly alter the statistical results, the repair of type 3 malformations by the primary abdominal-perineal pull-through technique without a preliminary colostomy gave the highest percentage of satisfactory and the lowest percentage of unsatisfactory results The term "satisfactory" is used in a broad sense but, in general, it indicates adequate intestinal and urinary control and the

TABLE 4 *Associated anomalies*

Vertebral deformities	10	Cloaca	2
Undescended testicle	9	Urethral diverticulum	1
Congenital heart disease	7	Hydronephrosis	1
Tracheo esophageal fistula	6	Thymus cyst	1
Nonfunctioning or absent kidney	6	Pharyngeal pouch cyst	1
Cleft palate or hare lip	5	Coarctation aorta	1
Hypospadias	4	Meckel's diverticulum	1
Congenital megacolon	4	Encephalocele	1
Mongolism	4	Omphalocele	1
Absent penis	3	Urethral valves	1
Malrotation of colon	3	Renal ectopy	1
Intestinal stenosis	3	Double vagina	1
Absent phalanges or limb	3	Patent urachus	1
Club foot	3	Amentia	1
Ectopic ureter	2	Horseshoe kidney	1
Absent auditory canal	2	Torticollis	1
Hydrocephalus	2	Anophthalmus	1
Bicornuate uterus	2	Bifid scrotum	1
Exstrophy of bladder	2	Absent testicle	1

TABLE 5 *Results*

Type	Management	Total	Dead	Satisfactory	Unsatisfactory	No Follow up Available
I	Dilation	17	1	7	1	8
II	Incision and dilatation	5		1	2	2
III		77	22			
A	Abdominal-perineal	11		8(73%)	1(10%)	2
B	Perineal	17		8(47%)	5(30%)	4
C	Colostomy, then perineal or abdominal perineal	22		12(57%)	4(18%)	6
D	Primary failure, colostomy, then repair again	5		5(100%)	—	—
IV	No repair	1		—	—	1
Totals		100	23%	41%	13%	23%

absence of urinary complications Satisfactory results were obtained in 41 per cent of the cases while 13 per cent were unsatisfactory Followup study was not available in 23 per cent of the cases Complete followup study of these remaining cases might considerably alter the results, however, of those cases with followup, there is general agreement with the results offered in the literature The known mortality rate for the series was 22 per cent and most of these deaths were due to associated anomalies and not to an operative procedure All of these deaths occurred before the age of four months

There are those who advocate management of the problem of anorectal malformation by a primary colostomy with repair later,[4, 5, 13, 17] and likewise there are many authors in favor of a primary abdominal-perineal approach[7, 8, 9, 18, 19] The perineal approach is usually reserved for the relatively short defects of less than 1 5 cm[4] When a colostomy is used, a "double-barreled" one is recommended to prevent the spilling-over of fecal material into the distal loop[5] One of the primary reasons for making this analysis was to determine whether or not fecal stream diversion by a preliminary colostomy would help achieve a higher percentage of successful rectourinary fistula repairs There was no appreciable difference in the number of successful repairs attained in the 22 cases treated either with or without colostomy prior to the time that initial repair of the defect was undertaken Also, there were a few failures of repair with each method used In contrast, and with but one exception, those who developed or still had a rectourinary fistula after an unsuccessful initial attempt at repair remained in that condition throughout subsequent repairs until a colostomy was made Therefore, although a preliminary colostomy does not appear to affect the success of the initial repair, it does contribute greatly to achieving success in the repair of the remaining or secondary rectourinary fistulas associated with anorectal malformations

The final answer as to the best attack on the intestinal malformation will be left to the general surgeons, our plea is that adequate *preoperative* lower urinary tract evaluation be made in the male patients so that the proper surgical approach might be made for the particular type of malformation present Certainly a high intestinal urinary fistula could not be managed adequately through a perineal approach

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COMPARATIVE STUDIES OF UROGRAPHIC MEDIA

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The introduction of urokon, miokon, hypaque and renografin recently by pharmaceutical houses is in answer to requests from physicians for an improved intravenously administered urographic medium. How well do these substances compare with older media in quality of the urogram and in the freedom from serious and/or annoying side reactions? In order to evaluate the efficiency of these substances, a study of over 2000 injections is now being reported. One of us (D. C.) supervised and had recorded any reactions which occurred during or after the intravenous injection. Both of us examined the films together recording the results in three categories: good, fair, or poor.

At University Hospitals intravenous pyelograms are done without prior preparation of the patient, i.e., no cleansing enemas, no fluid restriction. All patients are questioned in regard to previous allergic history and specifically about response to previously injected urographic substances. If no allergic history is obtained 0.5 cc of the selected medium is injected into an antecubital vein. The remainder of the solution is injected over a three-minute period if no reaction occurs within one minute. When symptoms of sensitivity are elicited, an intracutaneous test is performed. If the skin test is positive, the patient is considered a poor risk for intravenous injection of an organic iodide, and it is therefore not given. The usual preliminary film of the abdomen prior to injection, as well as films at specified intervals following the injection were done in this study.

RESULTS

Two thousand one hundred twenty-two patients were studied both from the standpoint of reactions to the contrast medium and the quality of the films that were obtained. Table 1 gives a breakdown on the total number of patients, the number of patients with reactions and the percentage of reactions for each of the contrast media used in this study. It is interesting to note that diodrast and renografin produced the least reactions, 6.05 per cent and 6.4 per cent respectively. Miokon had the greatest percentage of reactions, 49 per cent. This was due to the high incidence of flushing, and a bitter or metallic taste complained of by the patients.

Tables 2 and 3 give a breakdown of the types of major and minor reactions which were present in this study. It is interesting to note that aside from the flushing and bitter taste noted by patients when miokon was used and the pain in the arm noted by patients when neo-iopax was used, the predominant reaction of all of the contrast media was nausea and vomiting.

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Material utilized in this study was generously supplied by Mallinckrodt Chemical Works, Schering Corporation, E. R. Squibb and Sons, and Winthrop Laboratories.

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TABLE 1 *Reactions with various urographic media*

Contrast Media	Total No of Patients	No of Patients with Reaction	Percentage
Urokon, 70%	774	73	9 3%
Diodrast 35%	644	39	6 05%
Neo iopax 50%	179	29	16 2%
Miokon 50%	155	76	49 0%
Renografin 76%	235	15	6 4%
Hypaque 50%	135	22	16 29%

TABLE 2 *Major reactions*

Contrast Media	Nausea	Vomiting	Vein Cramps	Difficulty Breathing	Urticaria	Cardiovascular Collapse	Death
Urokon 70%	29	24	8	1	9	0	1
Diodrast, 35%	32	15	0	0	4	1	0
Neo iopax 50%	6	1	24	1	0	1	0
Miokon 50%	20	1	2	0	2	2	0
Renografin 76%	7	4	1	0	1	0	0
Hypaque 50%	17	5	4	1	1	0	0

TABLE 3 *Minor reactions*

Contrast Media	Flushing	Metalic or Bitter Taste	Sneezing	Tingling	Itching
Urokon, 70%	1	0	1	0	0
Diodrast 35%	1	0	1	0	0
Neo iopax, 50%	0	0	0	0	0
Miokon 50%	29	27	0	4	1
Renografin 76%	8	2	0	0	0
Hypaque, 50%	7	3	0	1	1

TABLE 4 *Quality of pyelograms*

Contrast Media	Good	Fair	Poor
	%	%	%
Urokon 70%	70 8	24 6	4 4
Diodrast 35%	71 8	19 3	8 7
Neo iopax, 50%	59	21	20
Miokon, 50%	89	6 8	4 1
Renografin, 76%	82 4	13 4	4 2
Hypaque, 50%	84 6	8 1	7 2

As mentioned previously, we graded the urograms into three categories good, fair, and poor We considered the pyelogram *good* when prompt and concentrated excretion of the radiopaque material occurred and when the urinary system was outlined sufficiently well to eliminate the need for retrograde studies

It was considered to be *fair* when the concentration of the contrast substance outlined the calyces and pelves sufficiently that a diagnostic statement could be made, yet the density was not comparable to that of a retrograde pyelogram If insufficient contrast medium was present to warrant a diagnostic statement the urogram was graded *poor*

We recognize that there are factors other than the contrast material which may be responsible for a grading of poor in this or any other study These include 1) the degree of renal insufficiency, 2) the state of hydration of the patient, and 3) the radiographic technique Whenever a poor film was obtained, an attempt was made to rule out causes other than the radiopaque material itself Most but not all could be related to 1 and 2 above

Table 4 gives a breakdown of the quality of pyelograms obtained with each of the contrast substances It is interesting to note that miokon, renografin and hypaque produce the highest percentage of good results Only renografin compares favorably with diodrast in the percentage of reactions It must be remembered, however, that the total number of patients studied with the newer materials is smaller than with urokon or diodrast Further studies are in progress and will be reported later

CONCLUSIONS

Two thousand one hundred twenty-two patients were studied using various urographic media Diodrast 35 per cent which has been used in this hospital for many years without serious side reactions was found to produce the fewest number of reactions The main objection to its use is that the quality of the urogram is inferior to that obtained with other media Whereas miokon, renografin and hypaque produce superior urograms, they also yield a higher incidence of reactions Only renografin approaches diodrast in the incidence of reactions, being 6 4 per cent whereas diodrast 35 per cent had 6 05 per cent

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FURTHER STUDIES OF REACTIONS DUE TO INTRAVENOUS UROGRAPHY

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Previously we have shown[1] that the number and severity of reactions following intravenous urography could be markedly reduced by the addition of 1 cc diphenhydramine (benadryl) to the urographic medium. In the VA Hospital, Bronx, N. Y., the use of iodopyracet (diodrast) has been discontinued due to frequent nausea and vomiting. At the present time we have been using sodium acetrizoate (urokon) and diatrizoate sodium (hypaque). We have also discontinued the use of sodium iodomethamate (neo-iopax) since it caused pain along the vein in the arm in too many cases.

Olssen[2] was among the first to demonstrate the effectiveness of benadryl in decreasing reactions in intravenous urography. Simon, Berman and Barald[3] demonstrated the value of another antihistamine, chlor-trimeton in reducing the number and severity of reactions. Our first study satisfied us that we could eliminate sensitivity tests which were time-consuming and unreliable and we have continued to use the safeguard of intravenous benadryl.

TABLE 1. *Sensitivity reactions to benadryl contrast medium mixture*

	Control Patients	Renografin Patients
Number of patients	137	123
Itching of skin or hives	1%	4.5%
Nausea or vomiting	1.4%	1%
Feeling of warmth	3%	1%
Shock reaction	0	0.8%

The use of a mixture of sodium and methylglucamine salts of diatrizoate (renografin) was described by Lentino, and others[4] who reported a marked decrease in reactions. They did not use an antihistamine in their study. They were pleased with the quality of visualization afforded by renografin. While we fully agree with the importance of satisfactory films, we have been primarily concerned with reducing the reactions to the lowest number possible. In addition the severity of such reactions has been our concern. It is the hope of all to avoid the occasional death that occurs following intravenous urography.

Using the same type of clinical material as in the first study, namely adult males from the general urologic ward, the paraplegic ward and the research unit for genito-tuberculosis, a comparative study was undertaken. In age these men

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[1] Wechsler, H.: N. Y. State J. Med., **56**: 401, 1956.

[2] Olssen, O.: Acta Radiol., **35**: 65, 1951.

[3] Simon, S. W., Berman, H. I. and Barald, F. C.: Ohio State Med. J., **50**: 247, 1954.

[4] Lentino, W., Zeitel, B. E., Jacobson, H. G. and Poppel, M. H.: J. A. M. A., **161**: 606–609, 1956.

varied from 22 to 80 On alternate weeks all patients who underwent intravenous pyelography were given hypaque or urokon with 1 cc benadryl, or renografin with 1 cc of benadryl was used At the end of six weeks the results were tabulated

The use of renografin was not difficult and although the solution is viscous, a No 21 or 22 gauge needle was satisfactory It was not necessary to warm the solution since room temperature was found to be also satisfactory

As will be seen from table 1 there was no unusual decrease in the reactions following the use of renografin Use of this drug resulted in less patients having feeling of warmth but more had itching of the skin or hives The shock reaction which occurred was not severe and responded well to treatment

SUMMARY

A comparative study using renografin with benadryl in one series and urokon or hypaque with benadryl in the second series, has been made The number and severity of the reactions were about the same in both groups Renografin evoked more itching of the skin or hives but fewer patients complained of a feeling of warmth No technical difficulties were experienced in injecting any of the urographic media

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INDICATIONS FOR NEPHRECTOMY, NEPHRO-URETERECTOMY AND PARTIAL NEPHRECTOMY IN RENAL TUBERCULOSIS

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In Europe, at the end of the nineteen-forties, just before the era of chemotherapy, certain broad concepts concerning the treatment of renal tuberculosis were becoming generally accepted For instance, it was almost universally agreed that renal tuberculosis should not be operated upon in the parenchymatous, that is, the nondestructive stage

On the other hand, most urologists performed nephrectomy in unilateral destructive renal tuberculosis Although there were still many supporters of the doctrine of immediate nephrectomy, i e , nephrectomy as soon as possible after the diagnosis was established, yet so-called "néphrectomie opportune" began to gain more and more ground This means nephrectomy at the most suitable moment, when the patient had acquired the greatest possible resistance to the tuberculous infection

In order to attain this state many considered preoperative sanatorium treatment necessary, a course which Thomas, in the United States, recommended as long ago as 1928 It was considered especially advisable in cases with coexisting extraurogenital tuberculous lesions, for more and more urologists thought nephrectomy should not be performed in such cases until these lesions were under control It should be emphasized that some urologists, such as dos Santos in Lisbon and Fey in Paris, hesitated to perform nephrectomy in early and especially in symptomless, cases of renal tuberculosis They kept such cases under observations and surgical treatment was based on the development of the disease

In many countries sanatorium treatment for patients with renal tuberculosis was not available, but in Denmark, Great Britain, Switzerland and Sweden sanatorium treatment was being given to an increasing extent For example, in 1948, we established in Gothenburg a unit for urogenital tuberculosis at Rävlanda sanatorium, where our patients are hospitalized for treatment All the urological examinations, operations, and x-ray examinations, other than those of the lungs, are carried out at Gothenburg's Sahlgrenska Hospital, where the patients are hospitalized for a few days for urological examination, generally every two or three months

After the introduction of chemotherapy, the indications for nephrectomy gradually changed considerably

Many urologists, among whom I would particularly mention Lattimer, have been able to show that with chemotherapy it is possible to achieve clinical, and in some cases, even anatomical healing in renal tuberculosis This required prolonged treatment of a year or two years with so-called combined chemotherapy

Read at annual meeting of American Urological Association, Pittsburgh, Pa , May 6-9, 1957 in the opinion of several urologists the most effective form is triple drug therapy (PAS, INH and streptomycin)

An important factor in the achievement of good results from this treatment is renal function, for if this is diminished one cannot expect a sufficiently high concentration of the drugs in the urine If function is good there is no reason why the results should not be equally good whether the kidney contains one lesion or more, provided these are connected with the renal pelvis so that they are in contact with the urine Where the lesions are isolated from the renal pelvis, for example by a stricture in the neck of a calyx, the bacteriostatic drugs cannot exercise any appreciable influence Another reason for this is that the blood supply to such foci is often insignificant

What are the indications for nephrectomy? One definite indication is the self-nephrectomized, so-called "cement kidney" As has been pointed out, especially by Dodson and Hanley, the tuberculous lesions in such kidneys do not heal and these kidneys, being foci of tuberculosis, constitute a dangerous threat Tuberculous pyonephrosis, especially if secondarily infected, is another definite indication for surgery and so are all kidneys with severely impaired function in which advanced tuberculosis usually exists However, if the decreased renal function is caused by a stricture of the ureter, and the kidney is not too much destroyed, one should not perform nephrectomy, but resect the stricture and repair the ureter instead

Social and economic conditions may sometimes intervene in determining the indications for nephrectomy For example, if conversion has not occurred in spite of prolonged chemotherapy, and the patient is not able to continue medical treatment for a still longer period, the course of the disease can sometimes be shortened by nephrectomy, even if this means the sacrifice of a large portion of healthy renal parenchyma

In the pre-chemotherapeutic era opinions differed as to the advisability of removing a tuberculous ureter at the time of nephrectomy for renal tuberculosis The advocates of this operation maintained, among other reasons, that ureteral tuberculosis certainly often heals after nephrectomy but that this healing is in many cases very slow Meanwhile, tubercle bacilli may be discharged from the ureter into the bladder to maintain a tuberculous lesion or cause re-infection

Many thought ureterectomy was especially indicated when a stricture was present in the lower part of the ureter, as this prevented free drainage into the bladder, and hindered healing of the ureteral tuberculosis, and, as the ureter is often dilated and sometimes distended in these cases, there is a danger that the ligated free end of the ureter will fail to heal and may break open to discharge its contents into the operative wound and infect it A similar problem exists in the presence of a vesicoureteral reflux, and there may be the added complication of the development of a urinary fistula in the loin wound For many years I have usually always performed nephro-ureterectomy in such conditions, and also in all conditions with pronounced tuberculosis of the ureter

To me, the introduction of chemotherapy did not seem to justify departing from these indications as our knowledge of the effect of chemotherapy on tuberculosis of the ureter is still imperfect Further, I think it is always an advantage to remove as much tuberculous tissue as possible, as the added risk of removing the whole ureter by a separate midline incision is negligible It prolongs the operation only 20–30 minutes, but I have had no complications with this operation In the last 10 years I have removed the ureter in more than half of the nephrectomies performed Since nephrectomy is now performed only in advanced cases, and since the ureter is then usually involved, the result is that nephrectomy is now combined with ureterectomy in an ever-increasing number of cases (fig 1)

In 1948, Semb showed that with meticulous technique and the protection of chemotherapy it was possible to successfully carry out partial nephrectomy in renal tuberculosis This statement was received in Europe with great interest, and many leading urologists soon adopted this method of treatment (table 1)

However, the enthusiasm for this operation has decreased considerably, and several urologists, for example Cibert, have not performed a single operation of this kind in recent years, and I have performed only one in the last two years

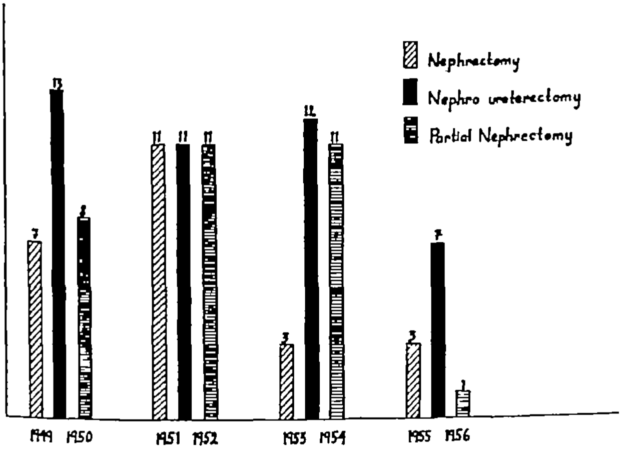

FIG 1 Operations for renal tuberculosis at Surgical Clinic I, University of Gothenburg, 1949–1956

TABLE 1 *Partial nephrectomy in renal tuberculosis*

	Number of cases	Operative mortality Number of cases	Late mortality Number of cases
Cibert (1955) France	48	5	—
Gow (1957) Great Britain	36	1	—
Kusunoki (1955) Japan	22	—	—
Ljunggren (1956) Sweden	29	—	—
May (1956) Germany	31	1	—
Puigvert (1957) Spain	39	1	5
Rakovec (1956) Yugoslavia	42	—	—
Semb (1956) Norway	160	—	3

Some reasons for this changed attitude were the high operative mortality in some series, and the complications which sometimes occurred after operation, such as urinary fistula, hemorrhage and cessation of function of the remainder of the kidney, which sometimes made its removal necessary But the main reason for the restrained attitude towards this operation were the good results obtained by medical treatment Thus it was found in many cases in which partial nephrectomy was carried out after prolonged chemotherapy that the tuberculous lesions had healed, or that the signs of healing were so pronounced that it was to be expected that they would have healed completely with continued chemotherapy

In Germany, the pathologist Singer has examined the specimens from 45 cases where partial nephrectomy for tuberculosis had been carried out by Alken, Boshamer, May and myself Singer found that in 15 the renal tuberculosis was healed, in eight there was productive renal tuberculosis in the course of healing, and in 22 the renal tuberculosis was not healed

In Gow's series the pathological report showed

	Cases
No evidence of tuberculosis	8
Healed tuberculosis	13
Inactive tuberculosis	3
Moderately active tuberculosis	2
Active tuberculosis	14

It is very interesting that several authors have independently reached the conclusion that it is "sealed-off" lesions which should be reserved for partial nephrectomy Other urologists consider that partial nephrectomy is also indicated in large cavities in open communication with the renal pelvis, even if conversion has occurred, and, among other reasons, because of the risk of stone formation and secondary infection (focal pyelonephritis)

Semb, on the other hand, still maintains the indications he gave in 1948 for partial nephrectomy, that is, that it should be performed in all cases where the

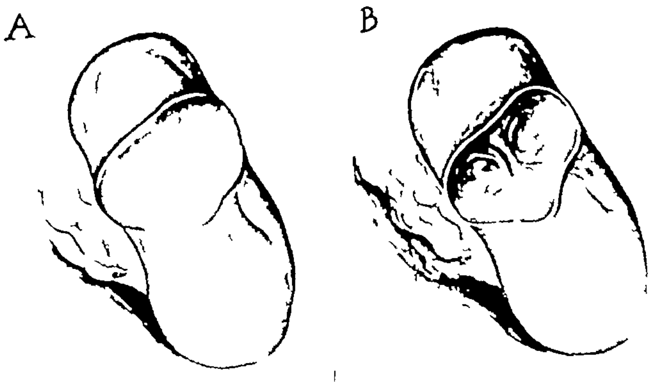

FIG 2 *A*, cavity size of hen's egg, with paper thin wall *B*, cavity size of hen's egg, after resection of paper thin wall (From Staehler, W Die Kavernotomie bei Nierentuberkulose (Medizinische, 27/28 943–945, 1954)

localized necrotic destructive foci in the kidney are limited to at most two of the three so-called divisions of the kidney

Finally I should like to mention that a method competing with partial nephrectomy for closed lesions—so-called speleotomy or cavernotomy—has been launched within the last few years It was introduced by Staehler in Germany, and has since been used with success by Aboulker in Paris The technique is extremely simple (fig 2) After a large lumbar incision and very careful exposure of the kidney in situ, the excluded lesion is evacuated by aspiration, after which the outer shell is incised, the caseous matter removed by means of a blunt curette or a small swab, 1 gm powdered streptomycin is placed in each emptied cavity, and a small polythene drain is fixed in it for subsequent daily instillations The lumbar incision is closed with the drain or drains passing through it

For the next 14 days daily injections of streptomycin or isoniazid are made through the drainage tubes

In all Staehler's seven cases and in six of Aboulker's seven cases healing took place by first intention I think this operation is to be recommended in closed lesions in a single remaining kidney

Thus surgical intervention on the tuberculous kidney, especially total nephrectomy, has diminished and surgery has had to focus on other fields in urinary tuberculosis In this way the ureter has come into the foreground Stricture of the ureter, which is most frequently situated in the lower part, may lead to impaired renal function, and so diminish the prospects of success with medical treatment, but what is more important it may lead to destruction of the kidney by hydronephrotic degeneration Many kidneys are now saved by resection of the strictured lower part of the ureter and reimplantation of the ureter in the bladder, thus re-establishing free drainage of the urinary tract In other cases, where a large part of the ureter is strictured, it must sometimes be replaced by an ileal loop In one case I removed the entire ureter and substituted an ileal loop for it, one end being anastomosed with the renal pelvis and the other with the bladder, and in this way saved a kidney which before the operation showed no definite contrast secretion on intravenous urography After the operation it showed good function and the patient has now been observed for over a year since the operation

Gentlemen I have here tried to present how we determine the indications for surgery in renal tuberculosis The future will show whether our present ideas are correct, or if we should go back to nephrectomy as the treatment of choice

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THE HEALING OF RENAL WOUNDS I PARTIAL NEPHRECTOMY

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Maximal conservation of functioning renal tissue is the major objective of surgical treatment for localized disease of the kidney Wide application of the operation of partial nephrectomy has been somewhat limited because of serious complications such as secondary hemorrhage and urinary fistula After the first partial nephrectomy by Czerny in 1887,[1] a number of these procedures were performed for tuberculosis and tumors The high incidence of complications led to virtual abandonment of the procedure until about 1930 when it was revived for the treatment of renal calculi and localized cysts or caliectasis In 1949, Dr Carl Semb[2] demonstrated that partial nephrectomy was feasible in carefully selected cases of renal tuberculosis and he reported an extremely low morbidity

A review of the available literature since 1930 reveals that complications of partial renal resection continue to occur despite improved surgical care and modern antibacterial therapy (table 1) In 819 cases of partial resection of the kidney for localized cysts, calculi, abscesses, hydronephrosis, caliectasis and benign tumors, the incidence of secondary hemorrhage was 3 4 per cent Urinary fistula occurred in 3 9 per cent and secondary nephrectomy was necessary in 2 5 per cent Thus a significant number of patients suffered severe complications or were subjected to the hazards and discomfort of a second major operation Similarly, in 384 cases of partial nephrectomy for tuberculosis collected from the available literature for the same period, there was an incidence of urinary fistula of 5 5 per cent, of secondary hemorrhage of 2 9 per cent, and secondary nephrectomy had to be performed in 3 4 per cent While the incidence of these complications is not high enough to prohibit the use of partial nephrectomy under certain conditions, it represents a constant threat which must be considered in selecting the best operation for a given case If the 226 partial nephrectomies for renal tuberculosis which were reported by Semb[3] are excluded, the incidence of urinary fistula in the tuberculosis series is 12 7 per cent, of secondary hemorrhage 7 per cent, and of secondary nephrectomy 8 2 per cent The explanation for the discrepancy between Semb's results and those of others is probably due to his careful selection of cases and his utilization of a technique whereby the amount of ischemic tissue left behind to undergo necrosis and atrophy is minimized The conventional type of wedge resection with approximation of the residual flaps by deep horizontal mattress or cobbler sutures must frequently result in necrosis of

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Read at annual meeting of American Urological Association, Pittsburgh, Pa , May 6-9, 1957

[1] Czerny quoted by Goldstein, A E and Abeshouse, B S , Partial resection of the kidney J Urol , 38 15, 1937

[2] Semb, C Renal tuberculosis and its treatment by partial resection of the kidney Acta Chir Scand , 98 457, 1949

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[illegible]

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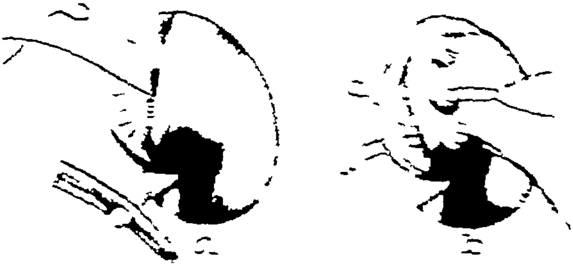

Fig. 1. [illegible]

[illegible]¹ The present study was designed to determine the normal course of healing after the conventional wedge type of partial nephrectomy and after another method which was thought likely to decrease the likelihood of tissue necrosis.

Three groups of animals were operated upon in the course of this study. The wedge type of resection was utilized in the first group of seven dogs. The animals were anesthetized with intravenous pentobarbital and the kidney exposed through a flank incision. The renal capsule was incised over the upper pole of the kidney and reflected to the lower limit of the line of resection. Hemostasis was secured during the resection by placing a Crafoord clamp on the vascular pedicle. A wedge of renal parenchyma was excised (fig. 1), removing with it the upper pole calyces and infundibulum. The collecting system was closed with a continuous suture of 5-0 chromic catgut. Hemostasis was obtained by identifying bleeding points after release of the clamp and ligating them with transfixion sutures of 5-0 catgut. The edges of renal parenchyma remaining after excision of the wedge were approximated by horizontal mattress sutures buttressed with tabs of perirenal fat. The capsule was closed over the incision with interrupted sutures of 3-0 catgut.

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[1] [illegible] E. F. and [illegible] H. J. [illegible], experimental [illegible] of postoperative [illegible] function. Surg., Gynec. & Obst. [illegible]

In the second group of animals, the renal parenchyma in the upper pole wa sectioned transversely to the long axis of the kidney after reflection of the capsul (fig 2, 1) Approximately one-third of the kidney parenchyma including the sam portion of the collecting system as removed by the wedge incision was excise The collecting system was carefully closed with a continuous 5-0 atraumati catgut suture Hemostasis was secured by individual suture-ligature of vessel visualized when the clamp on the renal pedicle was released After hemostasis wa

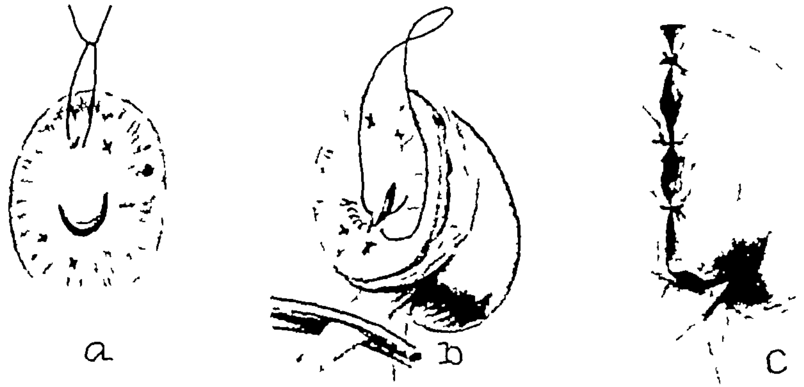

FIG 2 Technique of transverse type of resection Note a) method of obtaining hemostasis, b) closure of collecting system, c) closure of capsule

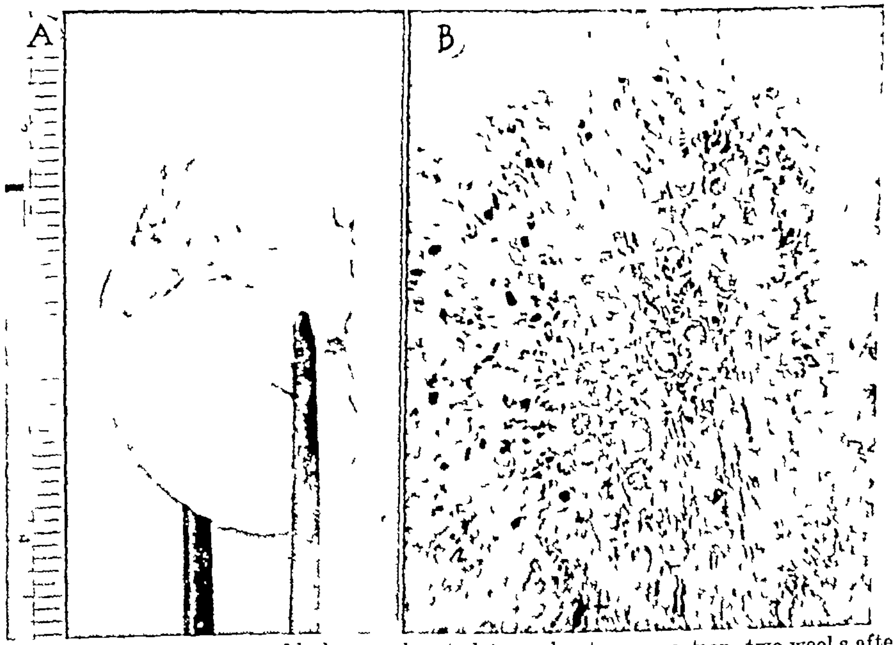

FIG 3 A, gross specimen of kidney, subjected to wedge type resection, two weeks after operation Note necrosis of flaps B, microscopic appearance of healing wedge resection at five weeks Note extensive necrosis and atrophy

accomplished a free graft of peritoneum was applied to the raw surface of the kidney by suturing the edges of the graft to the renal capsule

In the third group of animals, transverse resection of the renal parenchyma was accomplished exactly as in group 2, but the management of this group differed from group 2 in that no graft was utilized, the renal capsule (fig 2, *C*) being loosely approximated across the cut surface

Animals in each series were sacrificed at weekly intervals so that gross and microscopic evidence concerning the course of healing could be obtained over a period of seven to eight weeks Comparison of the wedge type of resection with the transverse method from the technical aspect emphasized the difficulty of closing accurately the renal collecting system when it was at the apex of a narrow wedge, whereas this was accomplished with ease on the broad, flat surface of the transverse section Visualization of bleeding points and accurate placement of hemostatic suture ligatures was likewise more difficult in the wedge type of resection

RESULTS

Except for superficial wound infections, no complications developed in any of the animals In the wedge resections examined one and two weeks after operation, the mattress sutures had cut deeply into the parenchyma and there was necrosis of the tissue distal to the sutures (fig 3, *A*) Later in the course of healing, it was apparent that there was scarring and fibrosis of and between the flaps with an area of atrophy several millimeters wide on either side (fig 3, *B*)

In the kidneys resected by the transverse method and on which a peritoneal graft was placed, there was evidence of a small hematoma beneath the graft in all but two cases Compression of the adjacent renal parenchyma was evidenced by a thin zone of atrophy just below the cut surface (fig 4) Thus, the desired effect of the graft (that of sealing the raw surface and promoting early healing) was lost

In the group of animals in which the capsule was loosely applied across the cut surface of the kidney after hemostasis was secured, healing proceeded without difficulty There was no evidence of necrosis or hematoma formation (fig 5, *A*)

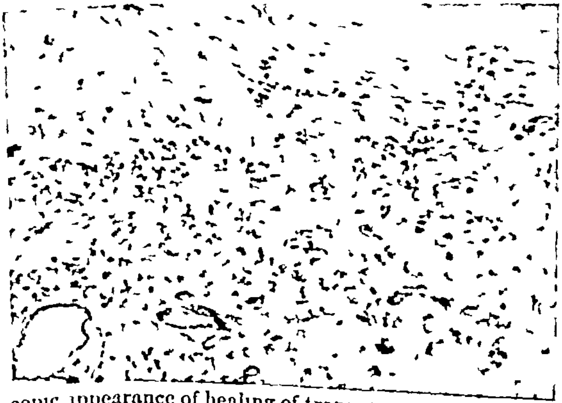

FIG 4 Microscopic appearance of healing of transverse resection with

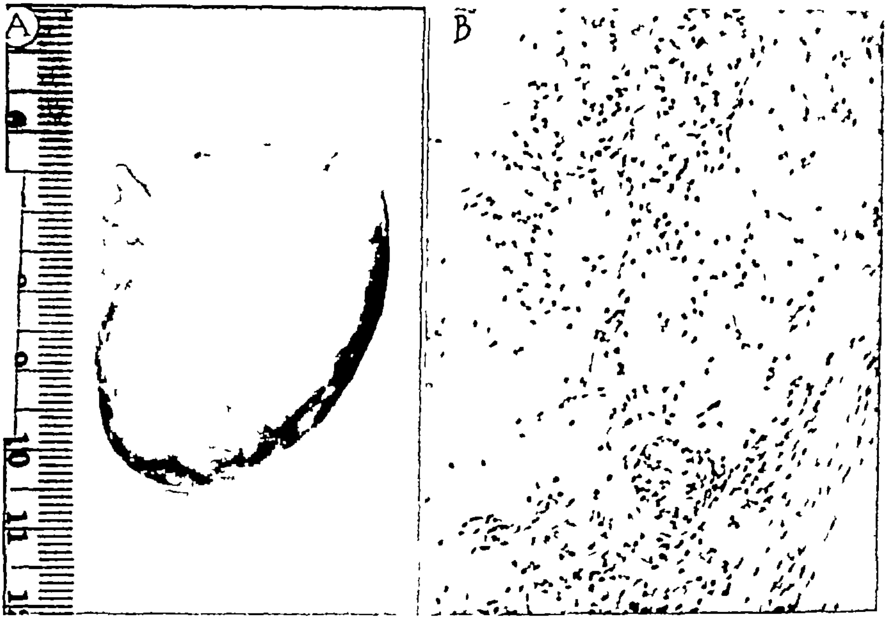

FIG 5 A, gross appearance of kidney, resected transversely, three weeks after operation Note absence of necrosis and atrophy B, microscopic appearance of healing transverse resection at seven weeks Note minimal atrophy of tissue

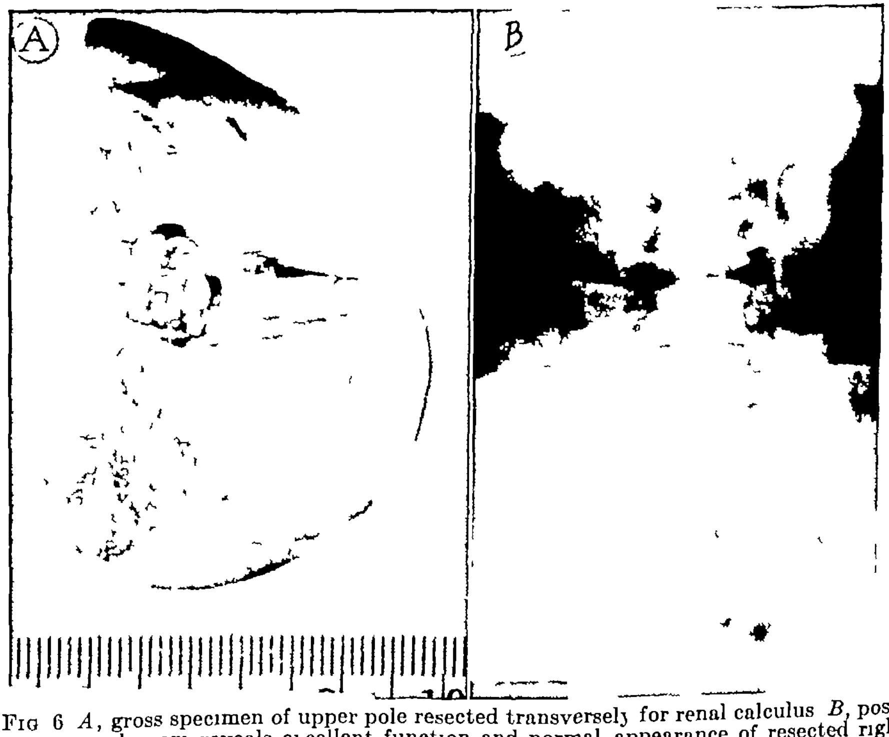

FIG 6 A, gross specimen of upper pole resected transversely for renal calculus B, post operative pyelogram reveals excellent function and normal appearance of resected right kidney

Microscopic examination of the tissue at various stages of healing after this procedure indicated minimal atrophy of the remaining renal parenchyma (fig 5, *B*)

CLINICAL EXPERIENCE

The technique of transverse resection has been used in five patients in the past six months It has proven to be entirely satisfactory in every respect The time required for the procedure has been decreased and blood loss minimized Figure 6, A shows the resected upper pole specimen, figure 6, *B* the postoperative pyelograms of a recent case

SUMMARY AND CONCLUSIONS

Partial nephrectomy by the conventional wedge type of resection appears to be likely to result in necrosis of renal parenchyma because of tension on the flaps of renal tissue caused by the mattress type of suture This necrosis may predispose to complications of secondary hemorrhage and urinary fistula as well as resulting in delayed healing and eventual fibrosis and atrophy

The renal parenchyma surrounding the portion of the collecting system which must be removed in partial nephrectomy contributes nothing to total renal function Removal of this tissue facilitates closure of the collecting system and the securing of hemostasis while minimizing the likelihood of the complications mentioned above

The use of a free graft of peritoneum to seal the raw surface of the resected kidney seemed attractive theoretically, but in practice resulted in hematoma formation between the graft and the cut surface of the kidney This resulted in pressure atrophy of the parenchyma beneath the graft

The transverse method of partial renal resection appears to facilitate the technical details of the operative procedure and permits rapid healing with minimal necrosis

The authors gratefully acknowledge the assistance of Dr Howard Rawnsley, Department of Pathology, University of Pennsylvania, in the evaluation of the microscopic sections in this study

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RENAL CONCENTRATING OPERATION AT LOW URINE FLOWS

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For the examination of the 'concentrating power' of the kidney reference has long been made to the specific gravity of the urine, as determined in one or more samples collected after 12 hours or more of hydropenia when the antidiuretic mechanisms of the body are presumably maximally excited It is recognized, however, that specific gravity is only a measurement of convenience, and that the proper reference is the osmotic pressure of the urine relative to the osmotic pressure of the blood, a datum which affords a direct measure of the osmotic gradient between urine and blood (31, 203f, 32, 325f, 612f, 34, 124f) Investigations carried out in this laboratory in recent years have afforded new information on the osmotic parameters in the dog and man (2, 19, 25, 33, 39), and the present study represents an effort to obtain additional information pertinent to the clinical evaluation of the concentrating operation

QUANTITATIVE ANALYSIS OF THE CONCENTRATING OPERATION

The following discussion pertains to the hydropenic state, when an osmotically concentrated urine is being excreted [1] In analyzing the operation by which this osmotic concentration is effected, it may be noted that as the glomerular filtrate passes down the tubule and various solutes (electrolytes, glucose, urea, etc) are reabsorbed, this solute reabsorption is accompanied by the reabsorption of water (perhaps generally in isosmotic quantities), but regardless of the relative magnitudes of solute and water reabsorption in all other operations, the fact that the final urine has a higher osmotic concentration than the blood demonstrates that in the net operation (and presumably at some point low in the nephron) water has been reabsorbed *without* an osmotically equivalent quantity of solute [2] This moiety of water reabsorption, originally designated as $T^{*}_{H_2O}$ (32, p 325), was subsequently called $T^{c}_{H_2O}$ by Wesson and Anslow (39), a more appropriate designation since the superfix *c* serves to identify it specifically with the concentrating operation

The quantity of solute-free water abstracted in concentrating the urine ($T^{c}_{H_2O}$) is given by the difference between the urine flow, V, and the simul-

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[1] The elaboration of a dilute urine has been discussed elsewhere (8, 17, 33, 34, p 108, 36)

[2] The site in the nephron where this solute free water is reabsorbed has not been demonstrated but the senior author leans to the belief that the collecting ducts are actively involved (29 32 p 325 216 317 33 34, p 122, 41) This concentrating operation may proceed continuously even during water diuresis, and recent evidence (3) indicates that it is not activated by the antidiuretic hormone

taneous *osmolal clearance*, C_{osm}.[3] The latter represents the volume of water required to contain all the constituents of the urine at an osmotic concentration equal to that of the plasma, and is calculated as $U_{osm}V/P_{osm}$, where U_{osm} and P_{osm} are the osmotic concentrations in urine and plasma, and V is the urine flow in cc/min. Thus,

$$(1) \qquad T^c_{H_2O} = \frac{U_{osm}V}{P_{osm}} - V = C_{osm} - V$$

the major terms being expressed in cc/min.

If no solute-free water were removed from the glomerular filtrate (if $T^c_{H_2O}$ = zero), the latter would, of course, remain isosmotic with the plasma, the osmotic U/P ratio (U_{osm}/P_{osm}) would be 1.0, and, in equation 1, C_{osm} would be equal to V. (This is essentially what is meant by the 'isosthenuric' state.) Under these circumstances, C_{osm} and V, when plotted against each other as in figure 1, would generate the bisector labelled 'isosmotic.' Only insofar as the urine volume is less than the simultaneous osmolal clearance does the kidney operate to conserve water and to maintain P_{osm} in a steady state. The greater the rate of solute-free water reabsorption, $T^c_{H_2O}$, per unit volume of urine, the greater will be the osmotic concentration of the latter; conversely, the greater the rate of solute excretion (osmolal clearance), the greater will be the quantity of water that must be reabsorbed to attain the same osmotic concentration.

At low urine flows (up to *ca.* 1.0 cc/min.), solute-free water reabsorption is limited by what has sometimes been called a concentration ceiling; this represents either the maximal urine osmotic concentration or the maximal osmotic U/P ratio attainable under maximal antidiuretic conditions. It is this limitation which is roughly reflected by a maximal specific gravity. (*A priori* one may anticipate that some limitation must be imposed on the reabsorption of water at low urine flows because otherwise the osmotic pressure would increase to physiologically inconceivable values and ultimately the urine would be concentrated to dryness.) Since P_{osm} is relatively constant, it is impossible at the present time to say which of these terms (U_{osm} or U_{osm}/P_{osm}) is physiologically more significant in limiting water reabsorption at low urine flows, though one may favor the osmotic U/P ratio because this expresses the actual osmotic gradient of water between the blood and urine.

Rearranging equation 1 and, for low urine flows, writing U_{osm}/P_{osm} = *a constant*,

$$(2) \qquad T^c_{H_2O}/V = U_{osm}/P_{osm} = \textit{a constant}$$

Under this limiting condition, $T^c_{H_2O}$ will increase in simple proportion to V and all observations will fall on line B in figure 1. The slope of this line (C_{osm}/V) gives the maximal U/P ratio; in the subject illustrated this ratio is 2.72.

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[3] It has been noted elsewhere (34, p. 195) that when U_{osm} and P_{osm} are determined by the freezing point method and converted to osmotic concentrations, these concentrations should be designated as osmolal (concentration per kg. of *water*) and not osmolar (concentration per kg. of *solution*). Consequently C_{osm} is properly called the *osmolal* clearance. The distinction between *osmolar* and *osmolal* arises from the circumstance that in mixed solutions great difficulties are encountered in equating osmotic concentrations per kg. of solution for different solutes because of differences in the molecular solution volume (or solution density) of these solutes.

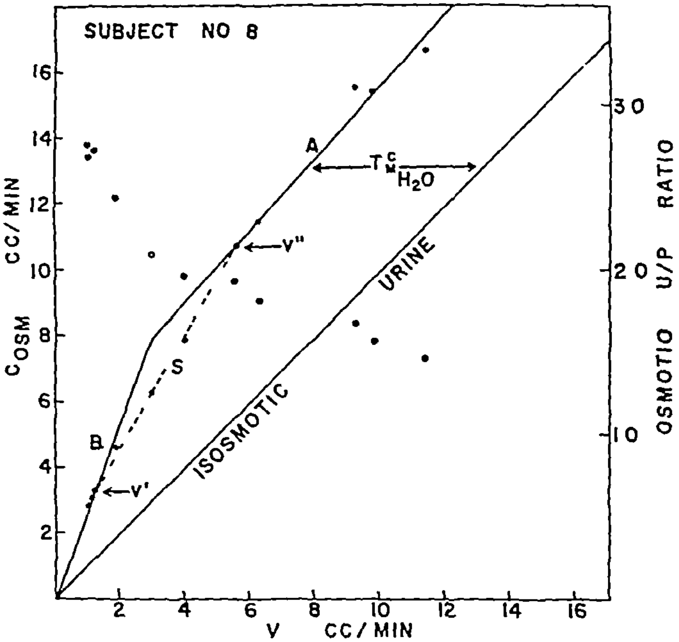

Fig 1 Evaluation of concentrating operation in normal hydropenic subject by mannitol diuresis Solid dots C_{osm} *vs* V Open circles osmotic U/P radio *vs* V

It has long been recognized that as the urine flow is increased (osmotic diuresis) in the antidiuretic state by the intravenous *administration of an unreabsorbed* solute (e g , mannitol, urea, etc), the osmotic concentration of the urine decreases and approaches that of the plasma as a limiting value In a detailed study utilizing mannitol in hydropenic subjects, Zak, Brun and Smith (42) have shown that under these conditions $T^c_{H_2O}$ attains an approximately constant value (see line A, figure 1) which they designate as $T^c m_{H_2O}$, and which presumably reflects a second limitation (maximal rate) in solute-free water reabsorption when the osmolal clearance is large $T^c m_{H_2O}$ is more or less characteristic of each individual As shown by line A in figure 1, $T^c m_{H_2O}$ in this subject, as measured at urine flows ranging from 5 2 to 10 7 cc /min , averages 5 2 cc/min

In any one subject the osmotic U/P ratio during increasing osmotic diuresis will conform to equation 2 at low urine flows, and at high urine flows where $T^c m_{H_2O}$ is approximately constant to the equation

$$\frac{U_{osm}}{P_{osm}} = 1 + \frac{T^c m_{H_2O}}{V} \qquad (3)$$

The present paper extends the study of Zak and associates to the transitional range between the oliguric state (line B), representing the maximal osmotic U P ratio, and the higher diuretic range (line A) in which $T^c m_{H_2O}$ is definitively measured This transitional range or 'splay' is marked S in figure 1 Information on the magnitude of urine flow which delimits this transitional range is pertinent not only to the application of '*concentration*' tests to the normal and diseased kidney, but also to such questions as the minimal water requirement on a high protein or high salt diet, the alleged 'osmotic diuresis' of the post-anuric state, and similar problems

METHODS

Our subjects, who presented no history of cardiovascular or renal disease, were selected from convalescent patients admitted for minor illness to the wards of Bellevue Hospital They ranged in age from 24 to 74 years Except where noted, they were on an unrestricted ward diet Before the test each subject abstained from all food and water for 12 to 14 hours and in addition received an intramuscular injection of 1 0 cc pitressin tannate in oil (5 pressor units) 4 hours before the start of the test to prevent possible psychogenic diuresis on moving from the ward to the Cardiovascular-Renal Research Unit, and any postural diuresis related to the return to the supine position after a variable period of ambulation (35) The tests were generally started between 8 00 and 9 00 a m

After the subject was in bed in the Research Unit, a control sample of blood was drawn from the antecubital vein and centrifuged at once, using minimal quantities of heparin dried in the syringe as an anticoagulant The bladder was emptied by catheterization and inflation with air without washout fluid, and the urine removed at this time was designated as U_0 After one or more samples of urine (U_1, U_2) had been collected, a priming dose of inulin (34, p 200) was injected into a convenient vein, and a sustaining infusion was established by a constant infusion pump A connection with a second infusion pump was established by introducing a needle into a rubber segment of the inulin infusion tubing and a slowly increasing osmotic diuresis was induced by the infusion of mannitol (5, 7 or 10 per cent) at rates ranging from 1 to 40 cc/min The mannitol concentration and rate of infusion were varied as needed to attain the desired urine flows Consecutive clearance periods were examined in which the urine flow ranged from control values of the order of 0 5 to 1 3 cc/min up to maximal diuretic flows ranging from 11 to 34 cc/min attained at the end of 3 or 4 hours

Inulin was determined by Roe's method as modified by Schreiner (30), sodium and potassium with a Baird flame photometer with internal lithium standard (13), creatinine by the method of Bonsnes and Taussky (4), urea by the Conway urease micro-diffusion method (15), and urine specific gravity by the gravimetric method Osmotic pressure was determined by the cryoscopic method of Wesson (38), at first by means of a Western Electric thermistor, Bowman null-point detector and Johlin cooling chamber, and later by the Aminco air-cooled apparatus of Bowman, Trantham and Caulfield (6) All osmotic concentrations are expressed as milliosmols per kilogram of water

RESULTS

Seventeen tests were made at oliguric levels in 12 subjects maintained on a mixed ward diet In 10 subjects the observations extended from oliguria to an osmotic diuresis of sufficient magnitude to permit measurement of $T^c_{mH_2O}$

In addition to the data reported in table 1, it may be noted that in the 12 subjects examined by us P_{osm} averages 282 mosm/kg (range 263 to 314), and U_{osm} averages 789 mosm/kg (range 614 to 975) In 82 subjects without cardiovascular or renal disease, ranging in age from 15 to 60 years, who have been examined in this laboratory since 1952, P_{osm} averages 283 ± 11 3 mosm/kg (range 260 to 318) [4] In 16 subjects subsisting on a ward diet reported by Smith (35) C_{osm} averages 2 29 cc/min per 1 73 sq m

TRANSITION FROM THE MAXIMAL OSMOTIC U/P RATIO TO $T^{c}_{H_2O}$

Our experiments were designed to start from the smallest postprandial urine flow attainable after 12 to 14 hours of hydropenia plus pitressin, and to describe in each patient what may be called the 'titration curve' generated by passing from line B upward through line A (fig 1) in consequence of slowly increasing osmotic diuresis

We have approached the graphical analysis of this region by plotting C_{osm} against V for each subject A straight line (B) was drawn between the zero ordinates and the point representing the greatest osmotic U/P ratio in that subject A second line (A) was drawn by visual fit through such points at high urine flows as showed linear regression of C_{osm} on V The highest value of V at which the osmotic U P ratio did not decrease by 0 1 or more below the maximal value is designated as V′ (column 9, table 1) In 15 observations on 11 subjects on a ward diet (counting each subject once only), V′ averages 0 97 ± 0 19 cc/min (range 0 78 to 1 31) per 1 73 sq m

Zak Brun and Smith (42) have shown that at intermediate to high urine flows the regression of C_{osm} on V is highly linear, regardless of the slope of the line [5] Our present experience with few exceptions, confirms this observation However, where the slope is greater or less than 1 0 T_{H_2O} never attains a constant value, but increases or decreases, respectively, as C_{osm} (or V) increases In such instances the only way to define the upper limit of 'splay' (S) in the titration curve is to extrapolate to the lowest value of V at which the regression of C_{osm} on V has become linear This minimal value of V is designated as V″ (column 10, table 1) In 13 observations on 9 subjects on a ward diet V″ averages 4 7 ± 0 54 cc min (range 4 2 to 6 0) per 1 73 sq m

In brief our data indicate that as the urine flow is progressively increased by osmotic diuresis during hydropenia, water reabsorption is limited by a maximal osmotic U P ratio up to an average flow of about 1 0 cc/min , thereafter this ratio begins to decrease, until at flows above 4 7 cc/min (in the average), the concentrating operation comes to be limited by the approximately maximal rate of water reabsorption hitherto identified as $T^{c}m_{H_2O}$.

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[4] These data include the subjects examined by Zak and associates (42) We are indebted to Dr Henry O Heinemann Dr Albert W Biggs and Dr David S Baldwin for the opportunity to include unpublished observations here

[5] The calculation of a correlation coefficient r for linear regression of C_{osm} on V, as performed by Zak and associates is improper because one variable V occurs also in C_{osm} (= $U_{osm}V$ P $_{osm}$ and the two terms contain simultaneous and correlated errors However, if the relation between C_{osm} and V is treated as the linear equation $U_{osm}V/P_{osm} = aV - b$ and both sides are divided by V the two variables U_{osm}/P_{osm} and 1/V are now independent and contain no correlated errors Hence within physiologically permissible limits, the regression coefficients *a* and *b* between the new variables, U_{osm}/P_{osm} and 1/V can be calculated and their standard deviations estimated by conventional statistical methods These calculations have not been carried out here because our present observations were not intended to test the linear nature *per se* of the regression of C_{osm} on V

CONSTANCY OF $T^{c}_{H_2O}$ AT INCREASING URINE FLOWS

In equation 1, $T^{c}_{H_2O}$ represents the *actual* rate (in cc/min.) at which solute-free water has been abstracted from the urine in order to concentrate it from an osmotic U/P ratio of 1.0 to the observed osmotic U/P ratio; this rate is mathematically determined by the measured terms, V and U_{osm}/P_{osm}. The expression $T^{c}m_{H_2O}$, however, implies that during substantial osmotic diuresis this rate attains a fixed, maximal value, presumably in consequence of some limitation within the concentrating mechanism which has a physiological and anatomical basis similar to those limitations that operate in other tubular transport systems ($Tm_{glucose}$, Tm_{PAH}, etc.).[6] All such 'maximal rates of tubular transport' imply (as a first approximation) the existence of a unitary process, freedom from intrinsic disturbance during measurement, and at least relative freedom from rapidly-acting tropic influences, and the expression 'maximal rate' discounts the anatomical diversity of the nephron population and other factors which might contribute to variability in total tubular transport.

Examination of figure 1 shows that the term $T^{c}_{H_2O}$ will be constant throughout a wide range of urine flow, and hence can accurately be characterized has having a 'maximal rate' ($T^{c}m_{H_2O}$), only when the slope of the regression line A is exactly 1.0, whereas in fact in some subjects (or in some tests on some subjects) the slope may be greater or less than 1.0 (as shown in column 7, tables 1, 2 and 3 of Zak and associates, and in column 15 of our table 1), with the consequence that $T^{c}_{H_2O}$ continues to increase or decrease, respectively, with increasing diuresis. When a number of subjects (or tests) are considered, however, the observed slope averages close to 1.0 (1.033 ± 0.075 in table 1 of Zak and associates and 1.114 ± 0.115 in our table 1),[7] while in 35 out of a total of 52 subjects examined by Zak, and associates and ourselves the slope falls within the range of 1.0 ± 0.1. Therefore we accept, with Zak and associates, that though the reabsorptive operation involved in concentrating the urine appears to be characterized by a maximal rate, under certain circumstances (perhaps related to the rather unphysiological conditions of extreme osmotic diuresis required for its measurement) one or more unidentified factors cause the gross calculated value, $T^{c}_{H_2O}$, to increase or decrease more or less uniformly with increasing osmotic diuresis.

Two extremes with respect to slope in our data may be mentioned. In subject No. 4, the slope on a first test was 1.267 and $T^{c}_{H_2O}$ increased from 5.9 cc/min. (at V = 4.6 cc/min.) to 12.5 cc/min. (at V = 28.5 cc/min.). This extreme deviation was not observed in two repetitions of the test, when the slope was 0.9377 and 0.9832; in the first repetition $T^{c}_{H_2O}$ decreased from 5.46 to 4.21 cc/min., and, in the second, $T^{c}_{H_2O}$ remained practically constant at 4.5 cc/min. over almost as great a range of urine flow. (The three tests are averaged in table 1.)

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[6] The nature of the limiting factor or factors in tubular transport have not yet been identified in a single system, and probably in many systems they are statistical rather than singular.

[7] The range of variation in our data (0.894 to 1.269) is no greater than that observed by Zak and associates (0.83 to 1.16), despite the facts that our data do not extend over as great a range of urine flow and include more observations at lower flows.

TABLE 1 *Osmotic diuresis in hydropenic subjects premedicated with pitressin All data corrected to 1.73 sq m body surface area except columns 6, 7, 15 and 17*

1 Subject No	2 Sex	3 Age	4 S A	5 V	6 P_{osm}	7 U_{osm}/P_{osm}	8 C_{osm}*	9 V	10 V	11 $T^c_{m_{H_2O}}$	12 $T^c_{m_{H_2O}}$/100 cc C_{IN}	13 V Range	14 V Median	15 Slope	16 C_{IN}	17 Max sp gr †
		yrs	*sq m*	*cc/min*	*mosm/kg*		*cc/min*	*cc/min*	*cc/min*	*cc/min*		*cc/min*	*cc/min*		*cc/min*	
1	M	54	1.99	0.90	281	3.29	2.07	1.11								1.023
2	M	71	1.83	0.55	314	2.48	1.38	1.18								1.026
3	M	52	1.65	0.60	293	2.61	1.59	0.91	5.0	4.32	2.87	5.0–33.6	19.1	0.894	151	1.032
4	M	58	1.52	0.96	276	2.85	2.40	1.18	6.0	5.00	7.20	6.0–28.9	17.7	1.063	79	1.027
5	M	38			271	2.66					4.98			1.022		1.022
6	M	31	1.47	0.67	282	3.20	2.21	0.94	4.2	5.00	4.81	4.2–15.5	8.9	1.227	104	1.026
7	M	31	1.66	0.75	274	3.27	2.46	0.82	5.0	7.23	6.25	5.2–12.5	8.8	1.260	116	1.025
8	M	44	1.85	1.11	271	2.71	3.00	1.14	5.2	5.18	4.03	5.2–10.7	7.9	1.073	129	1.016
11	M	59	1.90	0.68	287	3.03	2.09	0.78	4.2	4.32	5.80	4.2–15.9	10.0	1.003	80	1.024
14	F	46	1.74	0.90	288	2.40	2.47	1.04	4.2	4.50	4.57	4.2–22.1	12.9	1.063	104	1.019
15	F	21	1.68	0.95	279	2.41	2.26	1.28	5.2	4.92		5.2–10.7	8.0	1.237		1.011
16	M	60	1.61	1.11	291	2.15	2.36	1.31	5.0	4.38		5.1–12.7	9.0	1.205		1.014
Mean		46.8	1.70	0.83	282	2.77	2.29	0.97	4.7	4.99	5.06	4.9–18.0	11.3	1.114	108	1.022
σ				0.19		0.36	0.47	0.19	0.54	0.85	1.26		1.0	0.1115	24	0.006
N		12	11	11	12	12	11	11	9	9	8		9	10	7	12

* Not all data simultaneous with V in column 5

† Simultaneous with V in column 5

In subject No. 13 (high protein diet not included in table 1) the slope was 0.807, and $T^c_{H_2O}$ decreased from 4.64 cc/min. ($V = 6.2$ cc/min.) to 0.93 cc/min. ($V = 24.8$ cc/min.). (A second test was not available.) We are unable to add anything toward the explanation of these anomalous slopes beyond what Zak and associates have said.

COMPARISON OF $T^c_{H_2O}$ IN DIFFERENT SUBJECTS

When the slope of the regression line A is significantly greater or less than 1.0, it is difficult to decide how to make a quantitative comparison of the concentrating operation in different subjects, since $T^c_{H_2O}$ does not in fact have a constant value. Observations made at the maximal urine flow attained in any one test will be exaggerated by whatever factor or factors contribute to the deviation of slope and are prejudiced by the arbitrary range of the imposed osmotic diuresis, which is determined by the arbitrary design of the clinical test. Zak and associates took for comparison the value of $T^c_{H_2O}$ when $V = 20$ cc/min., but many of our observations do not extend to urine flows of this magnitude because we have concentrated our efforts on lower flows in order to study the region of 'splay' in the titration curve. Since in both studies, however, the average slope for all subjects is close to 1.0 (Zak and associates = 1.033, this study = 1.114), and insofar as deviations of slope may be supposed to be randomly distributed above and below 1.0 and unrelated to any specific value of V, we may anticipate that the average value of $T^c_{H_2O}$ at any substantial value of V would be roughly comparable in the two studies. Table 1 therefore records the average value of $T^c_{H_2O}$ as calculated from *all clearance periods* falling within the rectilinear portion of the regression line. So calculated for 9 subjects on a mixed diet (counting each subject once only), $T^c_{H_2O}$ averages 4.99 ± 0.85 cc/min. per 1.73 sq. m. (The median value of V in these observations is 11.3 ± 4.0 cc/min.) This figure is to be compared with the figure 5.1 ± 1.5 cc/min. calculated by Zak and associates for 21 subjects when $V = 20$ cc/min. Possibly the most that can be said about this method of comparison is that the agreement between the two values indicates a significant degree of congruence in the data where a number of subjects are averaged, but the method leaves much to be desired when it comes to relating any one subject to a 'mean normal value' if the slope in that subject differs markedly from 1.0.

We have also examined the consequences of extrapolating the regression line in each subject to low values of V (the difference will be slight whether one chooses an arbitrary value of V or of C_{osm}) on the assumption that the 'best' physiological value may be attained in the lower range of urine flow. This is equivalent to saying that the factor or factors which cause the slope to deviate above or below 1.0 are negligible at low urine flows and introduce an increasing error as the urine flow increases. Extrapolation to $V = 1.0$ cc/min. gives an average value for $T^c_{mH_2O}$ in our 9 subjects of 4.33 ± 0.87 cc/min. per 1.73 sq. m., and extrapolation to $V = 0.0$ cc/min. gives an average of 4.20 ± 0.86 cc/min. per 1.73 sq. m. The variability between various subjects, as indicated by the coefficient of variation ($= \sigma/\text{mean} \times 100$), when all clearance periods are averaged (as described in the preceding paragraph) is 17.0 per cent, while for V = 1.0 and V = 0.0 cc/min this coefficient is 20.2 and 20.4 per cent, respectively. The differences in σ/mean are clearly not significant and therefore our data do not favor one method of calculation as compared with another.[8]

EFFECTS OF DIET

We had undertaken to examine the effects of diet on the maximal osmotic U/P ratio and $T^c_{m_{H_2O}}$ when we learned of the studies of Epstein, Kleeman, Pursel and Hendrikx (10), and thereafter we discontinued this part of our program.[9] These investigators have shown that as between a diet with 20 and 150 to 200 gm. of protein per day for 3 days, the maximal osmotic U/P ratio increased in the average (9 subjects) from 2.74 to 3.32, while $T^c_{m_{H_2O}}$ increased in the average (7 subjects) *from 5.0 to 6.4 cc/min per 100 cc of glomerular filtrate.* (The urine flow averaged 0.60 and 1.08 cc/min. on the low and high protein diets, respectively, a change in urine flow that is probably not sufficient, according to our present experience, to decrease the osmotic U/P ratio significantly below the maximal value.) These changes in concentrating capacity are demonstrable in subjects receiving pitressin by intravenous administration and hence must be referred to changes in the intrinsic activity of the concentrating mechanism and not to changes in the secretion of the antidiuretic hormone. The effect of protein is simulated by the ingestion of urea (48 gm./day), but not in short-period urea diuresis.[10] NaCl (20 gm./day) was without effect. We have qualitatively confirmed the effect of a high versus low protein diet with respect to maximal osmotic U/P ratio in 3 subjects, and $T^c_{m_{H_2O}}$ in 2 subjects, though our differences in protein intake were not as extreme as those of Epstein and associates and our functional changes were less marked.

Epstein, Kleeman and Hendrikx (9) have also shown that relative water deprivation for 3 days increases both the maximal osmotic U/P ratio and $T^c_{m_{H_2O}}$, whereas hydration with 5 to 6 liters of water/day for 3 days reduces both values, as measured during intravenous pitressin administration. In fact, Kleeman and Maxwell (18) report that chronic (psychogenic?) polydipsia may lead to reversible loss of concentrating power. Since pitressin administered intravenously does not increase $T^c_{m_{H_2O}}$ in hydropenic subjects (12+ hours of water deprivation) who were also infused with hypertonic (10 per cent) mannitol, it appears that hydropenia (of 12 hours duration) plus hypertonic mannitol elicits maximal secretion of the antidiuretic hormone (42), and it is inferred that the increase in $T^c_{m_{H_2O}}$ and maximal osmotic U/P ratio brought about by more prolonged dehydration reflects a change in the intrinsic activity of the concentrating mechanism.

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[8] The corresponding figures calculated per 100 cc of glomerular filtrate in 7 subjects are 5.06 ± 1.26 (average of all clearance periods), 4.15 ± 0.83 (extrapolation *to V = 1.0* cc/min.), and 4.06 ± 0.82 (extrapolation to V = 0.0 cc/min.).

[9] We are indebted to Dr. Epstein and his colleagues for discussing their studies with us and for permitting us to see the manuscripts of their papers prior to publication.

[10] It appears that in the rat (unlike man) urea has an immediate effect on concentrating capacity (16). This exaltation of the concentrating operation by urea appears to be the first specific physiological action demonstrated for this compound above the elasmobranch fishes.

The reports of Epstein and his colleagues confirm and give quantitative definition to numerous observations indicating 'adaptive' or cumulative changes in the concentrating capacity of the kidney, and indicate that these changes are at the level of the renal tubule The increased concentrating power induced by dehydration may explain in large part the fact that pitressin administration *per se* to a hydrated subject does not always duplicate the effects, in respect to concentrating power, of dehydration or dehydration plus pitressin, as reported by West, Traeger and Kaplan (40)

MAXIMAL OSMOTIC U/P RATIO

As shown in table 1, the maximal osmotic concentration of short period urine samples in 12 subjects on a ward diet examined by us averages 789 mosm/kg (range 614 to 975), and the maximal osmotic U/P ratio averages 2 77 ± 0 36 (range 2 15 to 3 29) These figures are lower than those reported by others[11] Many urine concentrations reported by Koranyi, Lindemann, Steyer and Bugarszky (cited by Hamburger (14) and Bottazzi (5)) range from 1100 to 1200 mosm/kg McCance (21) obtained average maximal concentrations of 1110 to 1380 mosm/kg in 3 subjects, ranging in age from 20 to 30 years, who had been deprived of water for some 20 hours Gamble (12) in 'life-raft' studies with young male volunteers who thirsted for 4 days cites an average figure of 1400 mosm/kg

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From the statements of Sargent and Johnson (28) one might infer that the average maximal osmotic U/P ratio on a high and low protein diet in subjects examined by them was 5 22 and 3 0, respectively, but the basic analysis of their data involves extrapolation to an 'obligatory' urine volume on each diet, a step so hazardous for physiological reasons as to cast doubt on the validity of the subsequent calculations Moreover the use of an exponential equation to relate osmotic U/P ratio and V, especially with data collected under different conditions and at widely separated times, ignores possible independent variations in $T^c_{m_{H_2O}}$ and maximal osmotic U/P ratio, variations in splay in the osmotic titration curve, and variability of $T^c_{m_{H_2O}}$ itself with V

Taking P_{osm} = 283 mosm/kg., the data cited above would indicate maximal osmotic U/P ratios of 3.88 to 4.25 (Hamburger (14)), 3.92 to 4.87 (McCance (21)), 4.95 (Gamble (12)), 3.30, 3.30 and 3.63 (Miles and associates, avgs. (22)), and 3.80 (Frank and associates (11)). West and associates (40) report an average P_{osm} of 292 and maximal U_{osm} of 1000 mosm/kg. in 5 subjects, giving an average osmotic U/P ratio of 3.53. Epstein, Kleeman, Pursel and Hendrikx (10) report an average osmotic U/P ratio in 5 subjects on a mixed diet of only 3.32.

Except in the data of Miles and associates, the subjects reported above were presumably relatively young and physically active persons who were in an optimal state of nutrition, but it is impossible to pinpoint any deficiency in these respects in the hospitalized subjects examined by us. We gave pitressin tannate in oil 4 hours before the patient (who had for a period been ambulatory) lay down in bed in the Research Unit with the hope of eliminating the diuretic effect of the supine position (35) as well as any possible psychogenic diuresis. This measure may not have been effective, or it may be that differences in the state of nutrition, habitual fluid intake and other factors contribute more than has hitherto been suspected to variability in concentrating power in a mixed hospital population such as that from which we have drawn our subjects.

Correlation between $Tm^c_{H_2O}$ (calculated as the average for all clearance periods) and maximal osmotic U/P ratio is low (0.50). This suggests that the permeability to water of the nephron or collecting duct system distal to the locus of water reabsorption may vary more or less independently of the intrinsic activity of the water reabsorbing mechanism itself. It may, however, only reflect inadequacies in the calculation of $Tm^c_{H_2O}$, as discussed above.

MAXIMAL SPECIFIC GRAVITY

The several electrolytes and nonelectrolytes of the urine contribute differently per unit concentration to specific gravity (26) and osmotic pressure, and unidentified constituents contribute 20 to 30 per cent of the specific gravity (24). Comparison of specific gravity and osmotic pressure must therefore be empirical. Corcoran (7) reports a high correlation between maximal urine osmotic pressure and specific gravity (measured with a hydrometer) in overnight samples, the correlation coefficients ranged from 0.89 to 0.96 in subjects on an unrestricted diet and on diets in which salt intake was limited to 2 gm. down to 0.2 to 0.5 gm./day. This high correlation is not evident in older data (Hamburger and Bottazzi), and here one can be more confident of the accuracy of the urinometric measurement. Moreover, Miles, Paton and de Wardener (22) report poor correlation between specific gravity and osmotic concentration in protein-free and sugar-free urine samples, and the osmotic concentration is increased relative to specific gravity if urea is the predominant solute in the urine, as would be expected from the high osmotic pressure and low specific gravity of solutions of this compound (26).

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In our data on short period urine samples collected from pitressin-treated hydropenic subjects before the induction of osmotic diuresis, the correlation coefficient is only 0.50. It may be that this low correlation is related to some differential change in composition (diffusion of urea?) when the urine is left in the bladder overnight, but this supposition has no supporting evidence at the present time

EFFECTS OF AGE

Lewis and Alving (20) have shown that the maximal specific gravity (Addis-Shevky concentration test) in normal men over the age of 40 decreases with age, particularly after the age of 65 The overnight 12-hour urine flows in 103 subjects observed by Lewis and Alving were all less than 0 72 cc/min , and mostly below 0 60 cc/min , and from our present experience this range of urine flow is not such as to decrease the urine osmotic pressure below the maximal value In view of the low correlation between specific gravity and osmotic pressure, Lewis and Alving's data throw no light on the effects of age on osmotic concentrating power Our data are too limited both in number and in respect to age distribution to throw any light on this question

Miller and Shock (23) have noted that the maximal inulin U/P ratio attained after the intravenous administration of pitressin is also reduced with age The inulin U/P ratio is indeterminately related to the maximal osmotic concentration of the urine because of variations in filtration rate, the excretion of NaCl and urea in consequence of differences in diet, etc , and at best the trend suggests an effect of age which invites further study Such studies must be made, however, with due reference to the long-term effects of diet and chronic state of hydration

SUMMARY

The limiting osmotic parameters determining the renal concentrating operation in the antidiuretic state were examined in 12 subjects (age 24 to 74 years) without cardiovascular-renal disease and subsisting on a ward diet Antidiuresis was induced by deprivation of food and fluid for 12 to 14 hours, and reinforced by the administration of 5 units of pitressin intramuscularly 4 hours before the test The maximal osmotic U/P ratio was determined at low urine flows (up to 1 3 cc/min) and thereafter the maximal quantity of water which could be reabsorbed by the concentrating operation was measured at high urine flows ranging from 11 to 34 cc/min induced by mannitol diuresis

The maximal osmotic U/P ratio in 12 subjects averaged 2 77 ± 0 36 (range 2 15 to 3 29) A maximal osmotic U/P appears to be maintained up to urine flows of 0 78 to 1 31 (avg 0 97) cc/min

An approximately maximal rate of water reabsorption ($T^{c}m_{H_2O}$) was first attained during osmotic diuresis at urine flows ranging from 4 2 to 6 0 (avg 4 7) cc/min $T^{c}m_{H_2O}$, calculated as the average of all clearance periods in which C_{osm} and V show mutual linear regression, averaged 4 99 ± 0 85 (range 4 32 to 5 18) cc/min per 1 73 sq m in 9 subjects, and 5 06 ± 1 26 cc/min per 100 cc of glomerular filtrate in 8 subjects The osmotic U/P ratio decreases as the urine flow increases according to the relation $U_{osm}/P_{osm} = 1 + \frac{T^{c}m_{H_2O}}{V}$, hence the osmotic pressure of the urine approaches that of the plasma at high urine flows

Between the limits of *ca* 1 and *ca* 5 cc/min in urine flow the osmotic titration curve is indeterminate and the osmotic U/P ratio remains unpredictable

Attention is called to the recent demonstration that the maximal osmotic U P ratio and $Tm^{c}_{H\ O}$ are increased on a high protein as compared with a low protein diet, and both functions are increased by prolonged dehydration and decreased by prolonged hydration

The osmolar concentration of the plasma in 82 subjects without cardiovascular-renal disease averages 283 ± 11 3 (range 260 to 318) mosm liter

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RECOGNITION AND MANAGEMENT OF TRAUMA TO KIDNEY

JOHN R LISKA

The subject of the traumatized kidney has been well documented in the surgical literature, some controversy exists between those who would manage the problem conservatively and those who believe in a more radical surgical approach In 1949, E J McCague reported on "Conservative Management of Renal Trauma " In the same year, H W McKay outlined the "Active Surgical Management of the Ruptured Kidney " Thus, the divergent views were discussed almost simultaneously with each viewpoint having its adherents

Injuries of the ureter, other than surgically produced, are relatively few in number In this series of 81 cases, there are no injuries recorded as such Two cases of ruptured pelvis are reported, one due to an automobile accident, the other an indirect injury sustained by lifting a rabbit hutch The management of the ruptured pelvis arouses no controversy, drainage is indicated at the outset

An evaluation of 81 cases from 1945 to 1955 is presented, representing 26 cases from the Westmoreland Hospital, Greensburg, Pa and 55 cases from the Mercy Hospital, Pittsburgh, Pa In this series, the conservative concept has been followed and the results were satisfactory

ETIOLOGY AND INCIDENCE (TABLE 1)

The etiological agents or conditions under which injury is sustained are determined largely by our daily pursuits The gathering momentum of a nation on wheels reflects itself in the etiological table wherein the vehicular accidents account for 21 of the cases, or 26 per cent Football injuries account for an equal number of traumatized kidneys The next in order of frequency were falls, with 13 cases recorded, or 16 5 per cent Industrial accidents were productive of 9 9 per cent, or 8 cases Of these, the mine injury produced by crush due to slate fall was the more common cause Sled riding was the causative condition in 5 cases The penetrating wounds accounted for 4 cases, or 5 per cent of the total Baseball, a sport of limited body contact, is represented by 2 cases One case of renal trauma is etiologically cited as spontaneous, indirect being due to unusual muscular exertion, associated with lifting a heavy object in which a rupture of the renal pelvis was produced It is not known whether or not hydronephrosis pre-existed The right kidney was involved 36 times and the left 45 times In this group 86 per cent occurred in the male and only 14 per cent in the female The period of activity is emphasized in age incidence whereby 62 per cent occurred in the ages between 2 and 30 The extremes are represented by the ages of 2 and 88

PATHOLOGICAL ANATOMY

Moritz, in his PATHOLOGY OF TRAUMA, has divided injuries to the kidney into 1) contusions and 2) lacerations with severance of pedicle or injury to the

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Read at annual meeting of American Urological Association, Pittsburgh Pa May 6-9 1957

TABLE 1. *Etiological agent*

	Number	Sex		Side	
		M	F	R	L
Football	21	21		6	15
Automobile	21	15	6	13	8
Fall	13	11	2	5	8
Industrial	8	8		4	4
Sled riding	5	4	1	4	1
Assault	3	3		1	2
Gun shot	3	3			3
Baseball	2	2			2
Kicked by horse	2	2		2	
Stab wound	2		2		2
Spontaneous indirect	1	1		1	
Total	81	70	11	36	45

vascular structures as an adjunctive. Contusion is represented as injury to the kidney without disruption of the calyceal system or without break in the renal capsule. Consequently, no extravasation of dye is demonstrated and no enlargement or mass is palpable. Laceration, on the other hand, implies either a simple break in the capsule or calyceal system, or gross anatomical disruption of the kidney, with extravasation of dye into the perinephric tissues. Severance of vessels at the pedicle or in anomalous position produces no change anatomically, but loss of function or infarction may be demonstrated. An occasional error in diagnosis is encountered where gross diagnosis has been made of a retroperitoneal hematoma suggesting severe laceration of kidney. One such case in this series came to autopsy when the pathologist made a gross diagnosis of renal trauma, but on the microscopic section, no extravasation of blood was found in the renal parenchyma. Consequently a revised diagnosis of hematoma of perinephric tissue was made, suggesting rupture of the small vessels in perinephric fatty capsule.

Physiologically, total loss of function, or localized diminution of function due to infarction has been most frequently encountered. The interpretation of this aspect has been neglected to some extent until the more liberal use of intravenous urography has pointed up the situation. In transrenal laceration the extravasation of dye is of course readily demonstrated on urography, providing a definitive diagnosis early.

SIGNS AND SYMPTOMS

The obvious history of injury was obtained in almost every case, except two cases of alcoholism where a reliable history was not to be had, the type of traumatic agent or condition being duly recorded. Severe shock was present in 12 cases, or 15 per cent. A mass was found on examination in 7 cases. Gross hematuria was noted by the patient or found on examination in 62 cases, or 76 per cent, while microscopic hematuria was found in 18, or 22 per cent. In one patient hematuria was not found Physical examination revealed superficial laceration or contusion of skin of the flank or lower rib cage in many instances, and in almost every case costovertebral angle tenderness or flank tenderness could be elicited The severely shocked or unconscious patient was catheterized to determine whether or not injury to the urinary tract existed and the presence of hematuria was always considered significant

DIAGNOSIS

The diagnosis was based on history of injury, hematuria, gross or microscopic, mass in the flank, costovertebral angle tenderness, excretory urography and retrograde pyelography The simple abdominal film was found to have limited usefulness and consequently was not used except in very rare instances Orkin states that of 19 cases in his series, evidence of injury was suggested in 4 cases and was entirely misleading in one case Intravenous urography was performed in every case soon after admission where systemic blood pressure of 90 mg mercury or more could be obtained These patients were routinely treated in the emergency room until shock had been combated, and transferred by the same litter to the X-ray Department where intravenous urography was done In some instances a direct transfer to the operating room was effected by the same litter Pyelographically, extravasation of dye into the perinephric tissues indicated transrenal laceration of the kidney, while distortion in the collecting system suggested an intracapsular or calyceal laceration

Nonfunction and reduced function were suggestive of either pre-existing disease or the result of vascular injury In many instances a repeated urogram was necessary to confirm existing findings or for re-evaluation The repeated urogram, it must be emphasized, was not used sufficiently or carried out beyond the routine time set by the ordinary roentgenological department It is planned in the future to extend pyelographic time beyond the ordinary suggested routine time, depending on the condition of the patient In some cases, it has been run to 2 hours The importance of establishing a functioning contralateral kidney cannot be emphasized too strongly

Retrograde pyelograms were done in eight cases, and are indicated in patients with persistent nonfunctioning kidney, diminished segmental function and distortion of calyceal systems, or in any questionable reading of the excretory urogram Pyelographically, four cases of unilateral hydronephrosis were found and in one instance, bilateral hydronephrosis

Associated intra-abdominal injury, particularly rupture of liver and spleen, require immediate exploration Harbach, Gibson, and Lynch perform peritoneal aspiration routinely to determine presence of blood in peritoneal cavity This procedure has not been employed in this series We, and our consulting general surgeons, have relied on the usual signs 1) rigid abdomen, 2) loss of peristalsis, 3) increasing pulse rate, 4) fall in blood pressure

Adams and Musselman describe a triad of injury to spleen and left kidney associated with rupture of left diaphragm It is their opinion that injury to one demands careful evaluation of the other two In our series, this triad has not been noted, but careful study indicates an x-ray of chest in future injuries to one of the three organs

TREATMENT

Treatment of the 81 cases is divided into 1) expectant and 2) operative Of these patients, 88 per cent were treated conservatively by bed rest, fluids, combating shock, antibiotics and sedation The urine was examined closely and healing was determined by normal intravenous urogram and negative urine microscopically Of these patients, eighteen (22 per cent) are included in the operative group, a total of 20 surgical procedures performed (table 2)

It must be noted that the conservative management has been immeasurably supplemented by the availability of blood for transfusion and by the liberal use of antibiotic therapy

ANALYSIS OF TREATMENT (TABLE 3)

A perusal of table 3 reveals facts worthy of consideration and comment In no instance was immediate or emergency nephrectomy performed Three nephrectomies were performed one, 15 days after injury, the second, 23 days, and the third, 3 weeks after trauma Obviously, nephrectomy was not possible in the immediate post-traumatic period due to severe shock and in every case it was delayed until proper evaluation could be made In two cases, packing was used to control bleeding at 10 days and at 19 days after injury, but it must be noted that one of these nephrectomies was accomplished five days later, indicating that packing was not sufficient and that secondary bleeding occurred

Drainage of the perirenal fossa was effected in three cases, immediately in two and in seven days in the third case However, nephrectomy was performed in three weeks in the third case for secondary hemorrhage In one instance, drainage of an infected wound which followed packing was accomplished 21 days after injury Evacuation of a perirenal hematoma was performed in one case, no further surgery was required A retroperitoneal hematoma was found at lap-

TABLE 2 *Surgical procedures*

Operative cases	18
Operations	20
Nephrectomy	3
Drainage	4
Packing	3
Evacuation of hematoma	1
Abdominal Exploratory	
Rupture of spleen	2
Rupture of liver	2
Bowel resection	1
Retroperitoneal hematoma undisturbed	4
Other Procedures	
Marsupialization of renal cyst	1
Removal of bullet from lumbar muscles	1

TABLE 3 *Analysis of surgical procedures*

Case No		Time Interval after Injury
1	Packing	10 days
	Nephrectomy	15 days
2	Packing	Immediate
	Incision and drainage of infected wound	21 days
4	Nephrectomy	23 days
6	Removal of bullet from lumbar muscles, lacerated kidney	10 days
7	Marsupialization of renal cyst	48 days
11	Packing	19 days
13	Hematoma, perirenal, removed	23 days
17	Laparotomy; retroperitoneal hematoma untouched	Immediate
24	Repair of ruptured liver, retroperitoneal hematoma untouched	Immediate
37	Perirenal hematoma evacuated	2 days
39	Laparotomy, rupture of spleen, renal contusion, liver rupture	Immediate
45	Drainage of renal fossa	Immediate
55	Drainage of perirenal abscess	3 months
59	Subdural hemorrhage, craniotomy, renal contusion	4 days
68	Laparotomy, rupture of bowel	Immediate
71	Drainage of renal fossa, rupture of pelvis	2 days
72	Laparotomy, retroperitoneal hematoma, rupture of spleen	Immediate
79	Drainage of renal fossa	7 days
	Nephrectomy	3 weeks

arotomy in four patients and left undisturbed in all instances because of the precarious general condition of the patient incident to severe intra-abdominal injury It was decided by the general surgeon that interference would have added to the total trauma of the intra-abdominal surgery and in every instance, the general surgeon was justified in his judgment One patient had a combined intraperitoneal injury consisting of ruptured spleen and liver, plus severe contusion of kidney Another had a ruptured spleen with perirenal hematoma, and the third a ruptured liver with perirenal hematoma The fourth had signs of intraperitoneal injury with no damage, except right retroperitoneal hematoma The literature records the dire sequelae of renal injury in terms of abscess or cyst formation, but in this entire series, only one of each was found, at 48 days and at 90 days, respectively Drainage of the abscess and marsupialization of a renal cyst were effective in obtaining a clinical cure in each instance However, it is only fair to state that a followup was not obtained on these patients, so that further judgment as to their renal status is unknown Contusion and gangrene of the bowel were encountered once, and a surgeon elected to resect the bowel, with fatal result

MORTALITY

Mortality figures remain significant on analysis Three deaths occurred in this series (3 7 per cent) Operative mortality was 11 per cent, or two of the 18 cases The third mortality is listed as nonoperative, the patient being admitted in irreversible shock and expired 3 hours later The two operative mortalities were incident to laparotomy and craniotomy and could not be considered deaths due to renal trauma It is interesting to note that not one death was attributed to renal trauma alone, the patients with renal trauma alone survived to undergo adequate study prior to surgery, except for the few instances already discussed

DISCUSSION

Management of renal trauma is contingent upon the survival of the patient in the immediate post-traumatic periods, it has been adequately demonstrated in my series and in others that survival from renal trauma is the rule and not the exception Study has indicated that a patient with renal trauma alone will survive and that restoration of renal function is to be expected in a great majority However, intra-abdominal injuries associated with renal trauma pose a perplexing problem and frequently tax the judgment of the general surgeon and urologist In light of the facts presented, it must be concluded that intraperitoneal injury should be attended first because time is on the side of the urologist, primarily due to the anatomical position of the kidney, and the only exception noted is profuse and uncontrolled bleeding This position is supported by the fact that of the 81 cases in this series, only two patients required immediate surgical intervention to control hemorrhage It has been stressed that retrograde pyelograms be made more frequently, and some subscribe to this position wholeheartedly However, with advances in excretory urography, more information can be obtained with minimum discomfort to the patient, by the use of higher concentrations of opaque media and the increasing use of delayed urograms Recently, much information in the so-called nonfunctioning kidney has been obtained by this method Particularly, the nonfunctioning kidney on a 45-minute excretory urogram may be a functioning kidney in two hours, and essential information may be obtained without further subjecting the already traumatized patient to instrumentation

CONCLUSIONS

A statistical study of 81 cases is presented

No injuries of ureter due to trauma are recorded in this series

Twenty operative procedures were performed on 18 patients

Mortality of 3 7 per cent in this series is recorded, with no mortality attributed to renal injury alone

Greensburg, Pa

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EFFECTS OF ANTIBIOTICS AND VACCINATION ON EXPERIMENTAL PYELONEPHRITIS

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Many urgent problems develop in the prevention and treatment of urinary infections In recurrent pyelonephritis and cystitis permanent cure is notoriously difficult to attain Too often, after apparently effective treatment, reinfection takes place

In addition to intensive antimicrobial therapy during acute episodes, various methods of management have been advocated—prolonged maintenance therapy, elimination of precipitating causes, and the prophylactic use of drugs and vaccines It was for the purpose of testing the value of autogenous vaccine and antimicrobial drugs in the prevention of urinary infection that we conducted this study Experimental pyelonephritis was produced in rabbits by the intravenous injection of bacteria following partial ligation of one ureter Some animals were given autogenous vaccine before the injection, others were given tetracycline for a short time before and after Rabbits were used since they are comparable to humans in susceptibility to pyelonephritis

EXPERIMENTAL METHOD

In each animal partial ligation of one ureter was performed under ether anesthesia, alternating right and left sides The rabbits, weighing 2 to 3 kg each, were equally divided as to sex The upper portion of the ureter was exposed through a midline abdominal incision and partially ligated with a 4-0 silk suture Uniform compression was assured by including the shaft of a No 23 hypodermic needle in the ligature (fig 1, *a*), the needle being removed after the knot was secured (fig 1, *b*) This method proved uniformly successful in producing mild to moderate hydronephrosis (fig 2) In our technique the ligature was left in place, differing from previous methods in which it was removed at subsequent operation [1]

Pure cultures of *Escherichia coli* grown on desoxycholate medium were used for intravenous injection Each animal received 1 ml of bacterial suspension containing approximately three billion micro-organisms In vitro tests had shown that these bacteria were sensitive to less than 10 μgm per cc of tetracycline Vaccine of heat-killed organisms was prepared in a Hopkins tube from the strain used to produce infection The completed vaccine contained approximately one billion killed bacilli per ml

Autopsy was performed on the experimental animals when they died or were killed [illegible] ys to four months after operation The abdominal and thoracic

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Re[illegible] meeting of *American Urological Association, Pittsburgh, Pa*, May 6-9 1[illegible]

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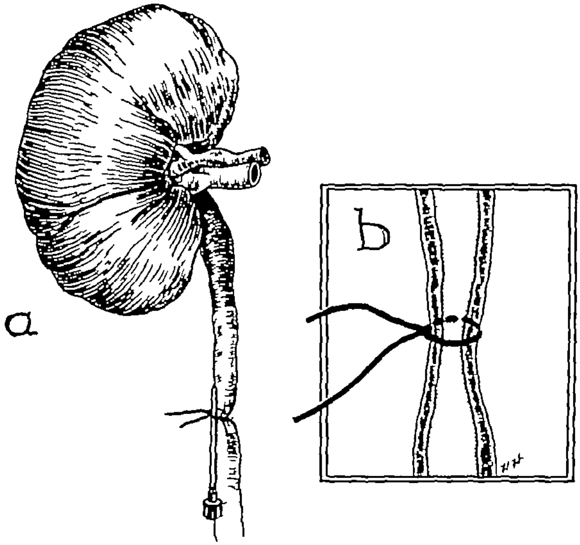

Fig 1 Method of partial ligation of ureter *a*, Silk ligature tied around ureter and shaft of No 23 needle *b*, Needle removed

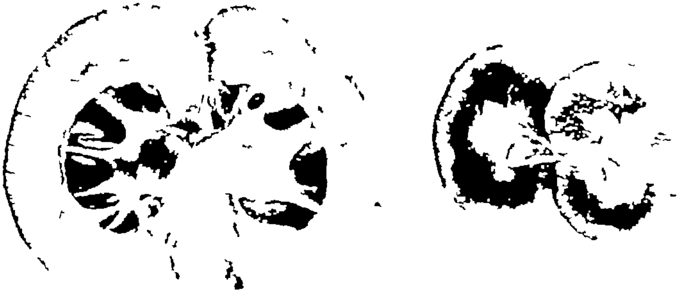

Fig 2 Moderate right hydronephrosis following partial ligation of ureter Normal left kidney One month postoperatively

organs were carefully inspected Microscopic sections of the kidneys were made in all instances, and of the lungs, liver, and spleen in many Pyelonephritis was graded severe, moderate, mild, or absent, on the basis of the severity and extent of infection determined by gross and microscopic examination of the kidney

SERIES 1

In an initial series of animals the efficacy of the method of producing pyelonephritis was tested In 24 rabbits, live bacteria were injected 24 hours after ureteral ligation In this group pyelonephritis was severe in the obstructed kidney in all but one animal in which there was no evidence of infection Mild

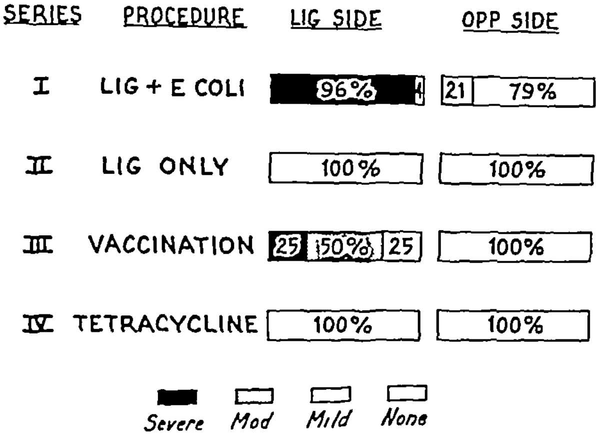

Fig 3 Incidence and severity of renal infection in four groups of experiments

infection developed in the contralateral kidney in five animals, the remainder were normal (fig 3) It is interesting that four of the five animals with bilateral renal infection died within two to five days In addition to the pyelonephritis, peritonitis was a contributing cause of death in two of the fatalities and intestinal obstruction from adhesions in a third

In six rabbits killed and autopsied 48 to 72 hours after injection, the obstructed kidney appeared normal, but on cut section innumerable small abscesses were seen in the pyramids adjacent to the calyces These early abscesses arose in the vicinity of small blood vessels In many sections the vessels contained bacterial thrombi In others bacteria were seen in capsular spaces of glomeruli and in neighboring tubules without inflammatory reaction Isolated bacteria were not present in animals autopsied more than 72 hours after injection

In six rabbits killed after five days the obstructed kidney was spotted with numerous cortical abscesses, and radial streaks of inflammatory reaction extended out from the tips of papillae into the cortex (fig 4) The pelvic wall was thickened at this stage

At two weeks infection was widespread in the obstructed kidney of six rabbits killed at this time Sections showed many areas of chronic pyelonephritis with necrosis and fibrosis There were also large abscesses, many of which had become confluent (fig 5) Some tubules contained pus cell casts

Two rabbits killed after one month, two after two months, and two after four months showed much the same chronic inflammatory reaction and extensive scarring of the obstructed kidney

Study of the contralateral kidney in this series showed mild infection in five rabbits The only notable findings were a few small abscesses about the pyramids There was no infection in the contralateral kidney in rabbits killed during or after the second postoperative week None of the other viscera showed evidence of infectio

Cultur e from specimens of urine obtained from renal pelves and bladder , but the results are not reported because they

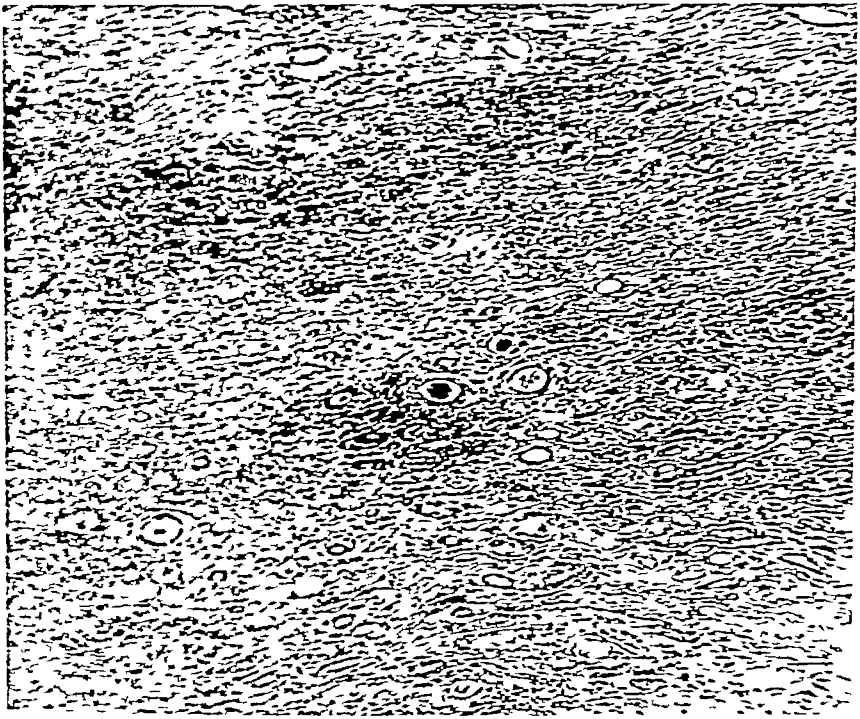

FIG 4 Acute pyelonephritis Obstructed kidney five days after bacterial injection (X110)

did not contribute to the diagnosis of pyelonephritis In most instances in which the microscopic picture showed evidence of infection, cultures of urine obtained from the renal pelvis were positive for the test organism No extraneous strains were recovered

One interesting observation was made in the early stages of infection in the obstructed kidney If no infection of the contralateral kidney was present, cultures of urine from the obstructed kidney were invariably positive, whereas cultures of urine from the bladder frequently showed no growth This apparently indicates that operative trauma or acute ureteritis led to complete temporary occlusion of the ureter After 48 hours cultures of bladder urine became consistently positive

SERIES 2

A second series of eight animals served as controls These rabbits underwent ureteral ligation without injection of bacteria Infection did not develop in any case (fig 3) The eight animals were killed in pairs, beginning one week after operation, and thereafter at intervals of about three weeks, the longest time being three months postoperatively Only the changes of progressive hydronephrosis with initial enlargement and subsequent atrophy were noted Cultures of the urine remained sterile

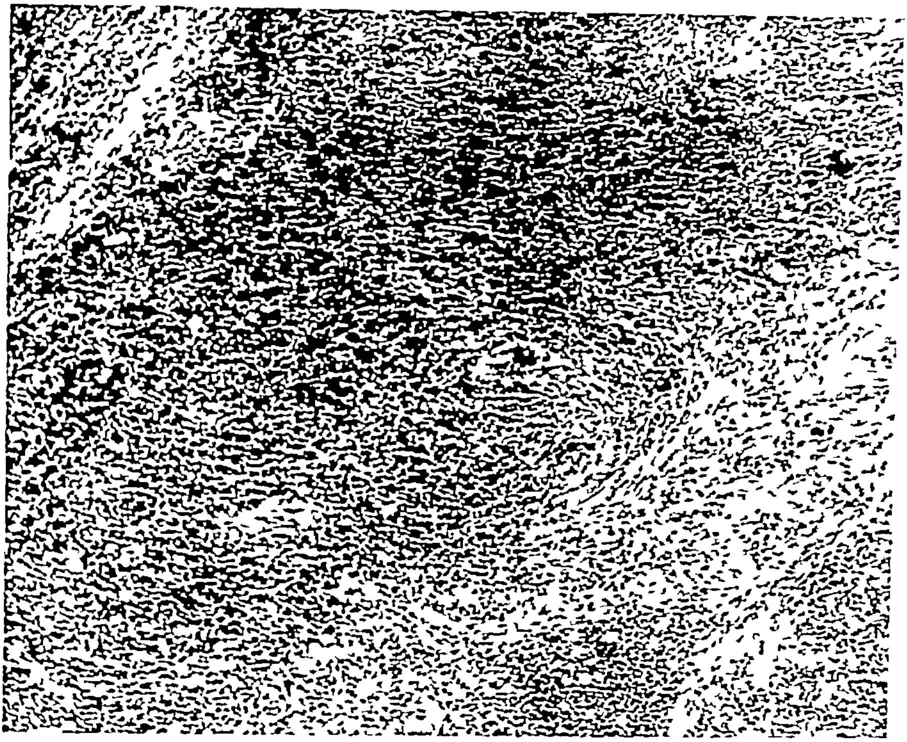

FIG 5 Chronic pyelonephritis Confluent abscess formation in obstructed kidney two weeks after bacterial injection (×110)

SERIES 3

A third series of 16 rabbits received autogenous vaccine prior to ureteral ligation Live bacteria were injected 24 hours later Starting six weeks' preoperatively each rabbit was given 1 ml of vaccine intravenously at 10-day intervals for four doses This dose is comparable to that which evokes an antibody titer in humans

The sixteen rabbits were autopsied at intervals of five days to one month after operation Infection was limited to the obstructed kidney, occurring in 12 animals Four showed changes of severe pyelonephritis similar to those in the unvaccinated animals Eight showed evidence of moderate pyelonephritis From two weeks to a month a few areas of scarring and a few collections of round cells were found The remaining four rabbits showed no evidence of pyelonephritis in either kidney, only hydronephrosis was present in the obstructed kidney (fig 3)

SERIES 4

The fourth series of 18 rabbits received tetracycline (tetracyn, Pfizer) intramuscularly, starting at the time of ureteral ligation which was 24 hours before live bacteria were injected intravenously Twenty-five milligrams of the drug were given every 12 hours for 10 doses This covered a period of five days When the 18 rabbits were killed from 48 hours to two months later, none showed any evidence of renal infection (fig 3) Only the changes of hydronephrosis were seen. All urine cultures were sterile

DISCUSSION

The pyelonephritis produced in these experiments was characterized by the typical lesions we have previously observed in man.[2] Although the earliest changes were best observed in the nonobstructed kidney whether or not obstruction was present the pathogenesis was similar and comparable to pyelonephritis observed clinically

Certain features of nonspecific renal infections are fascinating to observe yet difficult to explain. It is remarkable for example that recurrent infection is so often limited to one kidney Furthermore a kidney prone to recurrent infection is not always infected by the same bacteria in succeeding attacks Frequently there is a new or mixed infection. After repeated episodes of acute pyelonephritis a kidney may show few or no microscopic changes while one subject to asymptomatic chronic pyelonephritis is more usually the site of widespread destruction. Finally certain groups of bacteria for example various strains of gram-negative bacilli, have a peculiar propensity for infecting the urinary tract while others as the pneumococcus rarely do even in the presence of severe septicemia

The almost invariable development of pyelonephritis in the obstructed kidney rendered the method ideal for comparing methods of prophylaxis

Inoculation with a specific vaccine produced slight amelioration of the infection in many animals Vastly superior results were obtained by the administration of an antimicrobial drug to which the sensitivity of the test bacteria had been established. Although the vaccine was of discernible benefit under these experimental conditions the results were not comparable to the dramatic success attending the use of a specific antibiotic agent The experimental results in terms of numbers of animals used and the incidence of infection are statistically valid and significant

One might consider clinical application of vaccines when an infection is resistant to antimicrobial drugs yet several objections may be raised. First recurrent infection should produce antibody response if such response were an important factor. Second immunity to pyogenic bacteria produced by immunization is most transient Third different bacteria invade the kidney in recurrent infection. Clinical experience [illegible] indicate that these objections are valid

The development of renal infection in the antimicrobial-protected animal in the [illegible] obstruction and massive [illegible] proves that [illegible] the drug exerted a beneficial effect While our experiments were limited [illegible] drugs are effective [illegible]

The [illegible] may [illegible] into two considerations

[illegible] of urinary [illegible] ad- [illegible] and management of [illegible] ministration of antimicrobial agents at times when bacteremia or urogenous invasion is imminent?

2) Is the prophylactic use of antimicrobial drugs attended by undesirable effect?

Study of 350 cases after prostatectomy by Creevy and Feeney in 1949[3] and of 129 by Matthew Marshall in 1952[4] showed no reduction in the postoperative rise of temperature by prophylactic therapy Such clinical studies are difficult to evaluate because of the number of variables from patient to patient Since various agents have proven their therapeutic worth against practically every known pathogen of the urinary tract, it is difficult to discount their prophylatic value It would seem reasonable that if a drug can eliminate infection it can also prevent infection Under certain circumstances, for example, when there is precise knowledge of the nature of the threat, appropriate drugs would certainly seem beneficial An example of such circumstances is after operation in cases in which it has been impossible to eradicate a prostatic or urinary infection prior to removal of an obstructing prostate On the basis of our experiments it could be hoped that proper antimicrobial therapy would protect the kidney against the results of the inevitable introduction of bacteria into the tissue spaces and bloodstream at the time of operation

It should be stressed that in our experiments it was possible to prevent infection in both the presence of urinary obstruction and massive bacteremia In applying prophylactic therapy to clinical practice there is frequently an absence of obstruction and practically never such massive bacteremia

For the past five years we have employed a form of prophylaxis effective enough to appear beyond the possibility of chance We refer to the use of antimicrobial drugs to prevent postcoital urinary infection In women prone to develop pyelonephritis or cystitis after sexual intercourse a single therapeutic dose of a sulfonamide, tetracycline or chloramphenicol taken within two hours after coitus has eliminated the recurrent episodes in many instances

The same type of prophylaxis has seemed effective in reducing infection after urethral instrumentation, for example, urethral catheterization, cystoscopy, and the passage of urethral sounds, especially in the presence of urinary infection We are collecting information on a large number of cases with and without treatment so that the results can be compared

One fortuitous circumstance concerns prevention of urinary infection Most urinary infections are caused by the coliform group of micro-organisms which are susceptible to several drugs A generous assortment, with a wide spectral range, such as the sulfonamides, furadantin, tetracycline, and chloramphenicol offers many advantages Some are better concentrated in the tissues, others in the urine, some are better suited for prolonged administration, others for "spot" prevention Furthermore, if a patient is allergic to one, another may be employed

For long-term prophylaxis as when a retention catheter is in place and for maintenance therapy in recurrent acute and chronic urinary infections, sulfonamides and furadantin are especially suitable They are effective in small dosages, they are well concentrated in the urine, and are less prone to develop resistant strains of bacteria Furthermore, they do not disturb the bacterial flora of the large intestine

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For the immediate postoperative period, as following operation on an infected case, parenteral administration is desirable Of the broad-spectra drugs which lead to rapid, high concentration in the bloodstream and tissues there are penicillin-streptomycin combinations, tetracycline, and chloramphenicol Since bacterial resistance to streptomycin develops so rapidly it is not advantageous to use this drug for more than four days as a maximum

Any oral drug with a spectral range including the coliform bacilli is suitable to combat the transient showers of bacteria which may enter the bloodstream or urinary tract at the time of coitus or urethral instrumentation When used for this purpose the drug should be given in one full therapeutic dose

In the application of antimicrobial drugs for prophylaxis as well as in their therapeutic administration every effort must be made to avoid indiscriminate use Since so many promote the emergence of drug-resistant bacteria this factor should be taken into account in selecting drugs for prophylaxis In selecting drugs, too, they should be suited to combat the most common and likely invaders

One factor which causes difficulty is that in eliminating one type of organism encouragement is lent to the development of new pathogens In suppressing one group, way is made for others Hospital-acquired (nosocomial) infections lend increasing difficulty in control In many hospitals, strains of Pseudomonas, Proteus, and Micrococcus pyogenes have become widely disseminated and have caused serious infection since they are so frequently resistant to commonly used antimicrobial agents Unfortunately, in some instances overwhelming infection is so masked that profound sepsis is discovered only at autopsy [5]

With the development of new drugs and the improvement of old ones, toxic side effects due to the drugs are being reduced Under proper supervision serious reactions are now medical curiosities Allergic manifestations yield readily to treatment and are avoided by changing to another drug

SUMMARY

Experimental pyelonephritis was produced in rabbits by intravenous injection of Escherichia coli after partial ligation of one ureter In one group of animals autogenous vaccine was administered before inoculation, another group received tetracycline before and after injection Whereas vaccination lessened the severity of pyelonephritis in some animals tetracycline was found to be universally effective in preventing its development In the interpretation of these results clinical application is made concerning the prevention and treatment of urinary infections

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SQUAMOUS CELL CARCINOMA OF THE KIDNEY

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Although squamous cell carcinoma of the kidney is relatively rare, study of its distinctive pathologic features and unusual clinical manifestations is of interest and considerable practical significance Characteristics of this tumor include insidious onset and development, absence of any pathognomonic syndrome, frequent association with renal infection and calculi, direct parenchymal and perirenal involvement, remote metastatic dissemination rather than multicentric urinary epithelial implants, a high degree of malignancy and an extremely poor prognosis The extensive literature reviewed did not report any 5-year survivals

In an effort to study these and other characteristics of squamous cell tumors of the renal pelvis, a survey was made of 23 such cases encountered at the Mayo Clinic

GENERAL BACKGROUND

The first report of a case of squamous cell carcinoma of the kidney apparently was made by Hedenius[1] in 1878 Because of the conflicting terminology of the various pathologic diagnoses, confusion exists as to the exact number of reported cases In the past, some of the designations used, other than squamous cell carcinoma, have been epidermoid carcinoma, pavement epithelioma, sessile epithelioma, nonpapillary carcinoma, anaplastic carcinoma, epithelial pearls, epithelioma carcinoid, epithelioma and flat carcinomatous ulcer The most recent contributions by Dees[2], MacLean and Fowler[3], and O'Conor[4] make it probable that 132 cases have been reported to date

The comparative infrequency of squamous cell tumors of the renal pelvis was emphasized by Bell[5], who found only three carcinomas of the renal pelvis, none of which were composed of squamous cells, in a review of approximately 30,000 necropsies Hunt[6] compiled 318 surgically removed renal tumors at the Mayo Clinic and found 23 of the renal pelvis, only eight of which were of the squamous cell variety Walters[7] estimated the ratio of carcinoma of the renal pelvis to hypernephroma to be between 1 11 and 1 14

Accepted for publication June 3, 1957

Abridgment of thesis submitted by Dr Utz to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Urology

[1] Hedenius, P Fall af primar kräfta i venstra njurbäckenet och ureteren Upsala läkaref förh **13** 322–325 1878

[2] Dees, J E Prognosis of primary tumors of renal pelvis and ureter Tr Am A Genito Urin Surg , **47** 113–117 1955

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[5] Bell, E T A classification of renal tumors with observations on the frequency of various types J Urol , **39** 238–243, 1938

[6] Hunt, V C Papillary epithelioma of the renal pelvis J Urol , **18** 225–246, 1927

[7] Walters Waltman Malignant tumors of the kidney and pelvis of the kidney Five year cures following nephrectomy with partial or complete ureterectomy Surg , Gynec & Obst , **56** 445–447, 1933

Although nothing definite is known as to the exact mechanism responsible for the development of an epidermoid tumor in a normally transitional cell environment, clinical observation over the years has established certain impressions that serve in many instances to explain the phenomenon It appears that some form of irritation, resulting from chronic inflammation or the presence of stones, is responsible for the neoplasms A number of workers have published evidence supporting the relationship between long-standing inflammatory processes leukoplakia and the origin of renal squamous cell carcinoma[5, 13]

Other investigators however, have been disturbed that chronic pyelonephritis usually does not cause metaplasia and that leukoplakia occasionally is not associated with evidence of previous irritation[1, 17] They contend that some predisposition of the entodermal cell must exist or that these squamous cell epitheliomas are neoplastic developments from the embryonic inclusion within the renal pelvis of ectoderm that has found its way into the lower end of the primitive excretory duct by way of the cloaca

The causality between squamous cell carcinoma of the renal pelvis and calculi has been of interest to urologists and pathologists for years Martin and Mertz found calculi in 14 of 22 patients (63 per cent) who had epithelial tumors of the renal pelvis they observed that the average duration of symptoms caused by calculi was about 19 years and that of symptoms relative to tumor was 5 months Squamous cell carcinoma of the renal pelvis was associated with calculi in 30 of 57 case reports (52 per cent) collected by Gilbert and MacMillan[12] and in 48 of 100 case reports summarized by Gahagan and Reed[2] Park and Buzzanca[2] introduced sterile pebbles into the renal pelvis of 21 adult rabbits and induced a papillomatous growth in three instances

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The causality between squamous cell carcinoma of the renal pelvis and calculi has been of interest to urologists and pathologists for years Martin and Mertz[18] found calculi in 14 of 22 patients (63 per cent) who had epithelial tumors of the renal pelvis they observed that the average duration of symptoms caused by calculi was about 19 years and that of symptoms relative to tumor was 5 months Squamous cell carcinoma of the renal pelvis was associated with calculi in 30 of 57 case reports (52 per cent) collected by Gilbert and MacMillan[19] and in 48 of 100 case reports summarized by Gahagan and Reed [20] Pack and Buzzanca[21] introduced sterile pebbles into the renal pelvis of 21 adult rabbits and induced a papillomatous growth in three instances

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SQUAMOUS CELL CARCINOMA OF THE KIDNEY

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Although squamous cell carcinoma of the kidney is relatively rare, study of its distinctive pathologic features and unusual clinical manifestations is of interest and considerable practical significance Characteristics of this tumor include insidious onset and development, absence of any pathognomonic syndrome, frequent association with renal infection and calculi, direct parenchymal and perirenal involvement, remote metastatic dissemination rather than multicentric urinary epithelial implants, a high degree of malignancy and an extremely poor prognosis The extensive literature reviewed did not report any 5-year survivals

In an effort to study these and other characteristics of squamous cell tumors of the renal pelvis, a survey was made of 23 such cases encountered at the Mayo Clinic

GENERAL BACKGROUND

The first report of a case of squamous cell carcinoma of the kidney apparently was made by Hedenius[1] in 1878 Because of the conflicting terminology of the various pathologic diagnoses, confusion exists as to the exact number of reported cases In the past, some of the designations used, other than squamous cell carcinoma, have been epidermoid carcinoma, pavement epithelioma, sessile epithelioma, nonpapillary carcinoma, anaplastic carcinoma, epithelial pearls, epithelioma carcinoid, epithelioma and flat carcinomatous ulcer The most recent contributions by Dees[2], MacLean and Fowler[3], and O'Conor[4] make it probable that 132 cases have been reported to date

The comparative infrequency of squamous cell tumors of the renal pelvis was emphasized by Bell[5], who found only three carcinomas of the renal pelvis, none of which were composed of squamous cells, in a review of approximately 30,000 necropsies Hunt[6] compiled 318 surgically removed renal tumors at the Mayo Clinic and found 23 of the renal pelvis, only eight of which were of the squamous cell variety Walters[7] estimated the ratio of carcinoma of the renal pelvis to hypernephroma to be between 1 11 and 1 14

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Abridgment of thesis submitted by Dr Utz to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Urology

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[2] Dees, J E Prognosis of primary tumors of renal pelvis and ureter Tr Am A Genito Urin Surg, 47 113–117, 1955

[3] MacLean, J T and Fowler, V B Pathology of tumors of the renal pelvis and ureter Tr Am A Genito Urin Surg 47 69–100, 1955

[4] O'Conor V J The diagnosis of tumors of the renal pelvis and ureter Tr Am A Genito Urin Surg, 47 66–68, 1955

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[6] Hunt, V C Papillary epithelioma of the renal pelvis J Urol, 18 225–246, 1927

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Although nothing definite is known as to the exact mechanism responsible for the development of an epidermoid tumor in a normally transitional cell environment, clinical observation over the years has established certain impressions that serve in many instances to explain the phenomenon It appears that some form of irritation, resulting from chronic inflammation or the presence of stones, is responsible for the neoplasms A number of workers have published evidence supporting the relationship between long-standing inflammatory processes, leukoplakia and the origin of renal squamous cell carcinoma [8-13]

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Scholl[22] declared that renal stones should be removed as early as possible, not only to relieve pain and prevent destruction of renal tissue but also because in some cases it should prevent the formation of a malignant tumor

Hunt[6] observed that the degree of malignancy of squamous cell carcinomas of the kidney is usually high, with grades 3 and 4 predominating All of the 13 tumors reported by Melicow[23] were of either of these two grades Scholl and Foulds[24] pointed out that small zones of keratinization or pearl formation sometimes occur in papillary transitional cell epithelioma of the renal pelvis On the other hand, Oberkircher and associates[25] eliminated three cases in their series because of some papillary formation, although portions of these tumors contained squamous elements

Culp[26] recently emphasized that surgical treatment entails nephrectomy and only partial ureterectomy because renal squamous cell carcinoma, unlike the transitional cell variety, has no propensity to recur in the distal two thirds of the ureter or in the bladder Higgins[27] considered postoperative roentgen therapy to be advisable, although he observed no apparent reduction in the size of the tumor with preoperative radiation

MATERIAL AND METHODS

Case records for this study were selected from the clinical files of the Mayo Clinic, and the renal specimens were obtained from the files of pathologic specimens of the clinic A total of 175 kidneys with carcinoma of the renal pelvis encountered from 1907 through 1954 were examined

Each gross specimen was studied for the size, morphologic aspects and infiltrating characteristics of the tumors Sections for histopathologic study were made from various regions of the specimen, particularly the hilus, extracapsular tissue, junctional regions, areas suggesting leukoplakia, and each portion of the tumor demonstrating variations in gross structure

A total of 23 cases of squamous cell carcinoma of the renal pelvis were found The remainder of the series included transitional cell tumors and adenocarcinomas, which will be reviewed in a subsequent paper

CLINICAL DATA

The occurrence of these tumors in comparatively young patients is confirmed by this series, the average age was 54 years and 16 (70 per cent) of the patients were less than 60 The youngest patient was 42 years of age, and the oldest was 70 The predominance of men (20 of the 23 patients) was an unusual feature

The right kidney was involved in 13 patients and the left in 10

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Pain was a symptom in all instances and was the chief complaint of 17 patients (74 per cent) The pain was either sharp and colicky or dull, aching and constant in about an equal number of instances The presence of calculi bore no constant relationship to the character of the pain Thirteen (57 per cent) of the patients had pain in the flank, and the pain extended anteriorly in eight of these The pain was in the anterior renal region in six patients, extending posteriorly in four Three patients had epigastric pain and one had pain in the periumbilical region

Gross hematuria was noted by 11 patients (48 per cent), but it was the principal complaint of only three Five patients were aware of an abdominal mass, and two stated this was their foremost concern

One patient had the chief complaint of an unaccountable loss of 20 pounds in one year All but three patients had noted some degree of weight loss, in 15 instances, this amounted to more than 20 pounds in 6 months

Although 12 patients specified that their urinary tract symptoms had existed for six months or less, a substantial number (seven) had experienced either pain or gross hematuria for more than a year One patient, a 61-year-old woman, had been cognizant of an abdominal mass for a year The longest duration of symptoms occurred in a 47-year-old man who had noted intermittent severe colicky pains in the flank for 30 years In others, pain or hematuria or both had been present for 15 months to 20 years

In addition, many patients referred to a wide variety of abdominal or constitutional symptoms, principally constipation (40 per cent), anorexia (40 per cent), bloating or epigastric fullness (30 per cent), weakness and undue fatigability (38 per cent) and heartburn (22 per cent) Nine patients complained of frequency of urination or dysuria or both, but only three gave histories of chills or fever

General examination disclosed a palpable abdominal mass in 15 of the 23 patients, this usually was hard, irregular and immobile It was tender in 11 instances Low-grade fever was present in nine patients

Pyuria existed in all patients, this was grade 1 in eight patients, grade 2 in three, grade 3 in three and grade 4 in seven The grade was not mentioned in two instances A total of 19 patients had microhematuria, this was grade 1 in 13 instances, grade 2 in one, grade 3 in one and grade 4 in two The grade was not recorded in two patients

Values for blood urea were abnormal in only three of the 12 patients on whom the test was done The erythrocytic sedimentation rate was substantially increased in each of the nine instances in which it was measured, the average rate was 67 mm during the first hour (Westergren method)

Leukocytosis was present in 81 per cent of the patients on whom such counts were made The values for hemoglobin indicated that anemia was present in 70 per cent of the patients so studied

Urographic investigation was carried out on all but the initial patient, who was studied in 1907 A plain roentgenogram of the abdomen, or KUB, was made in two patients, excretory urograms in five, retrograde pyelograms in six and both excretory urograms and retrograde pyelograms in nine A pathologic condition was described in all these studies The preoperative diagnoses (more than one diagnosis being made in some instances) were as follows indeterminate renal neoplasm, eight cases, tumor of the renal pelvis, three, pyonephrosis, eight, tuberculous pyonephrosis, one, nephrolithiasis, seven and hydronephrosis, three

Exploration of the affected kidney was advised in each instance, and nephrectomy was accomplished in 22 patients In the remaining patient, the renal mass was so large and the perirenal involvement so extensive that no attempt was made to remove the tumor at operation, biopsy only being performed

A variable number of postoperative roentgen treatments were given to five patients

GROSS APPEARANCE

Considerable variation occurred in the gross appearance of these squamous cell carcinomas of the kidney The diameter of the lesions ranged up to 12 cm The size of the kidney also depended on the position of the tumor in the renal pelvis and the degree of obstruction it produced One huge hydronephrotic kidney, which was the size of a football and weighed 2,400 gm, contained a squamous cell carcinoma measuring 4 by 4 by 3 cm that obstructed the ureteropelvic juncture Multicentric implants occasionally occurred In two instances, the lesion developed in a calyx, leaving the renal pelvis unaffected

With one exception, all the tumors were entirely or in part solid, or nonpapillary One squamous cell carcinoma, a component part of a transitional cell carcinoma, existed exclusively as a villous growth measuring 2 5 by 2 by 1 5 cm that was attached to the renal pelvis by a broad pedicle Another specimen was predominantly villous and in six other tumors there were lesser amounts of villous formation, making a total of eight (35 per cent) of these squamous cell carcinomas that had some papillary features This was confirmed microscopically A few of the solid tumors presented necrotic disintegrating surfaces that might be confused grossly with villous structures

An outstanding observation at operation was the severe degree of fixation of the kidney and edema of the perirenal tissues caused by infection or by penetration of the capsule by tumor The intimate association of this neoplasm with infection is supported by this observation and by the occurrence of pyonephrosis in 15 of these patients

Gross extension of the tumor beyond the pelvis and parenchyma, with infiltration of the hilar structures, was observed in 19 instances This closely paralleled the microscopic findings Some of the tissues described at operation as involved included the hilar lymph nodes, duodenum, diaphragm, adrenal glands and the erector spinae and psoas muscles The estimated amount of actual destruction of the renal parenchyma caused by the tumor varied from 30 to 95 per cent In a few cases, a mass could not be identified in the parenchyma, the pelvis alone being involved

Extension to the upper 2 or 3 cm of the ureter by a large infiltrating mass at the ureteropelvic juncture was noticed in one specimen Leukoplakia could be identified grossly in four specimens, three of which contained renal calculi

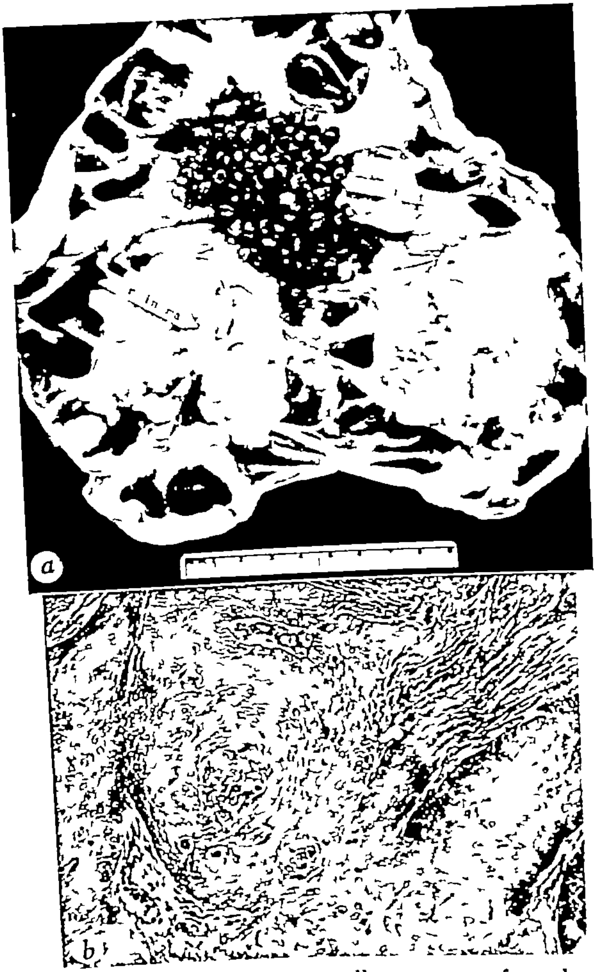

FIG 1 Grade 1 noninfiltrating squamous cell carcinoma of renal pelvis Patient was living and well 14 years after nephrectomy *a* Gross specimen demonstrating tumor, calculi and hydronephrosis *b* Note well differentiated character of tumor (hematoxylin and eosin, ×100)

Squamous cell carcinoma was associated with renal calculi in 13 of the 23 specimens (57 per cent) The calculi varied in number and size from small, solitary stones to multiple large calculi or those of the staghorn variety (fig 1)

MICROSCOPIC CHARACTERISTICS

These 23 tumors had, to varying degrees, some or all of the diagnostic histologic features of typical squamous cell carcinoma These features are too well known to warrant repetition here When the tumors were ulcerated or necrotic or were undergoing inflammatory degeneration, the core of some of the nests of neoplastic cells consisted of granular necrotic debris However, some measure of keratinization was present in all 23 tumors

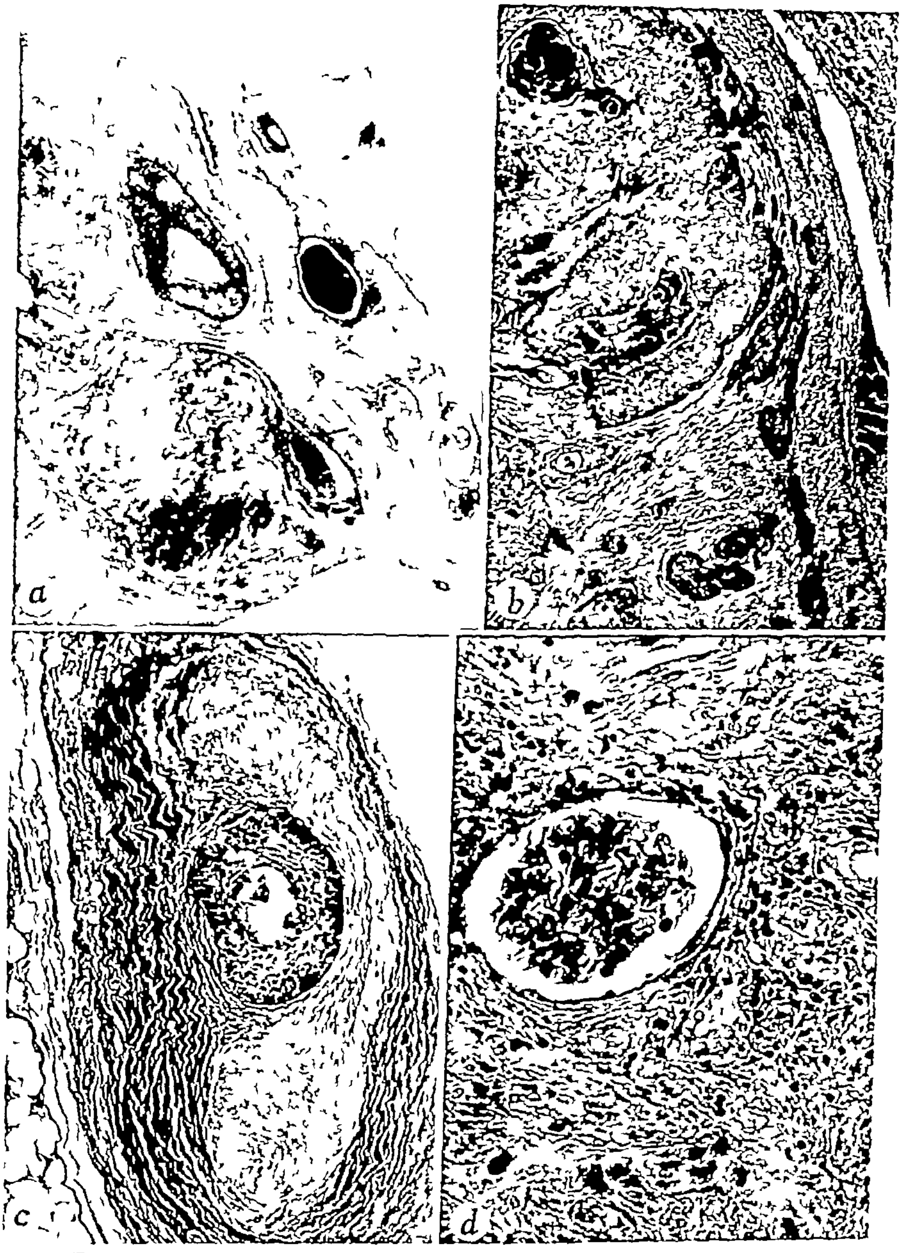

FIG 2 Hematoxylin and eosin sections of a grade 3 infiltrating squamous cell carcinoma of renal pelvis *a*, Hilus showing infiltration of renal vein, nerve and lymphatic vessels (×5) *b*, Involvement of vein (×50) *c*, Involvement of nerve (×50) *d*, Parenchymal involvement (×300)

Graded by the Broders method, these tumors exhibited a predominance of the higher grades of malignancy, one lesion was grade 1, three were grade 2, 10 were grade 3 and nine were grade 4

Vascular involvement of the hilar vessels was evident microscopically in 18

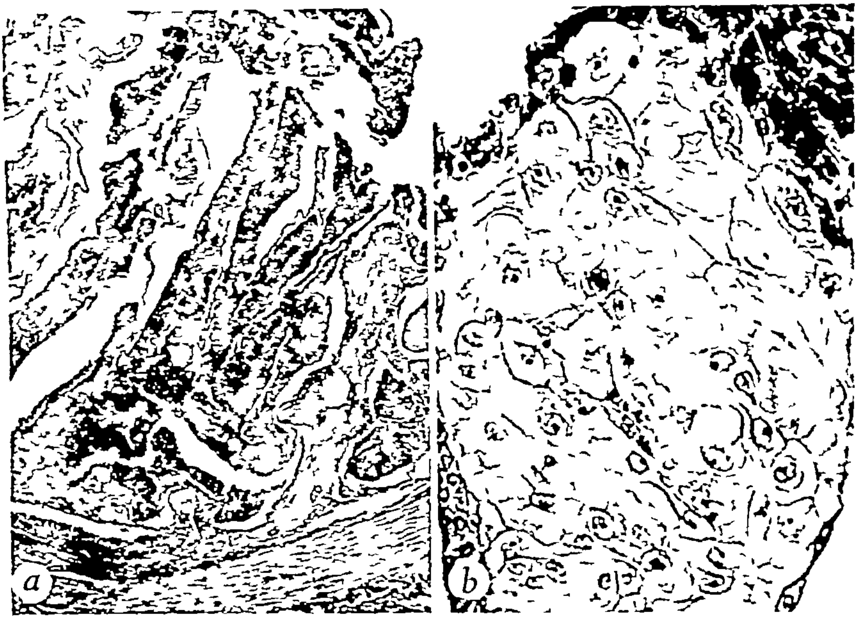

FIG 3 Coexisting noninfiltrating grade 3 transitional cell and squamous cell carcinoma in a patient living and well 15 years after nephrectomy *a*, Papillary transitional cell carcinoma (hematoxylin and eosin, ×30) *b* Island of squamous cell carcinoma in same tumor (hematoxylin and eosin, ×375)

cases (fig 2) Two of the five specimens in which vascular involvement could not be discerned showed infiltration of the muscles in the wall of the renal pelvis but no further penetration Extension beyond the submucosa had not taken place in the remaining three cases

Coexistence of squamous cell and transitional cell carcinoma was not rare (fig 3) Transitional cell carcinoma, predominantly of high grade, was associated in six cases (26 per cent), frequently being present in the same microscopic field or on the same papillary structures, the latter was evident in four of the six cases

RESULTS OF TREATMENT

One hospital death occurred in this series, representing an operative mortality of 4 per cent This patient died of bacteremia after nephrectomy done in 1920 for a large, grade 4, extensively infiltrating squamous cell carcinoma that had invaded all the principal vessels of the renal pedicle

Nineteen other patients have died As far as can be determined two of these 19 died of causes not related to the renal tumors One of these two patients died of coronary occlusion at 82 years of age, having survived $15\frac{3}{4}$ years after nephrectomy and radiation therapy for a combined squamous cell and transitional cell carcinoma, grade 3, of the renal pelvis that had penetrated through the muscular layer but not entirely through the renal pelvic wall into the hilar vessels During this 15 year interval he had been examined periodically at the clinic without evidence of recurrence The other patient died at home of a cerebrovascular

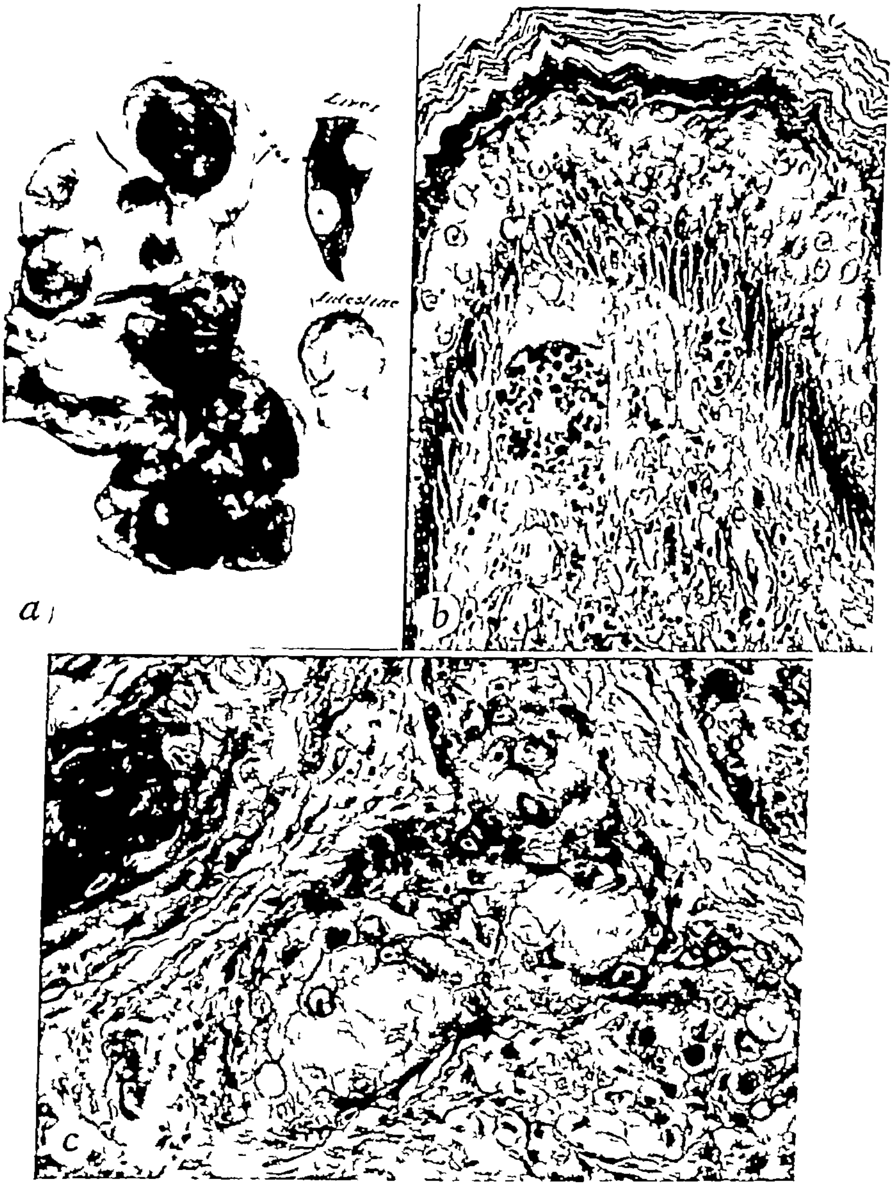

Fig 4 Grade 4 infiltrating squamous cell carcinoma in a patient who lived 6 weeks after nephrectomy *a* Gross specimen showing calculi and renal tumor almost completely replacing parenchyma, with two sites of metastasis *b*, Leukoplakia in renal pelvis (hematoxylin and eosin, ×300) *c*, Tumor showing high degree of malignancy (hematoxylin and eosin, ×200)

accident at 66 years of age, 4½ years after nephrectomy for a grade 2 squamous cell carcinoma with the same depth of infiltration as the tumor just described It could not be determined if this patient had any complaints suggestive of neoplastic recurrence

All the other 17 patients who died had deeply infiltrating lesions with vascular and frequent neural involvement in the hilus, parenchymal involvement and extension beyond the capsule were common This group of lesions included two grade 2 tumors, whereas seven were grade 3 and eight were grade 4 Only five of these 17 patients survived 1 year or more after operation One patient who had an obviously deeply infiltrating tumor lived 6⅚ years

Necropsy data were available on two of these 17 patients A 54-year-old man, who died 7 weeks after nephrectomy for a grade 4 extensively infiltrating tumor, had metastatic lesions in the lymph nodes of the renal fossa and in the liver and duodenum (fig 4) A 47-year-old man, who lived 2 months after nephrectomy for a similar squamous cell carcinoma, had widespread metastasis to the diaphragm, both lungs, spleen, sigmoid, the body of the second lumbar vertebra and the capsule and cortex of the contralateral kidney

Three patients were living and well at intervals of 15, 14 and 3 years, respectively, after operation The tumor in each instance was a noninfiltrating squamous cell carcinoma Despite the fact that two of these lesions were grade 3, the other being grade 1, the muscular layer of the renal pelvic wall was undisturbed in the three specimens None of these three patients had postoperative roentgen treatment

COMMENT

The fact that only 23 (13 per cent) of the 175 tumors of the renal pelvis treated surgically at the clinic during a period of 48 years were squamous cell carcinomas testifies to the singularity of this neoplasm It is worth re-emphasis that 87 per cent of these 23 tumors were in men The average age of the patients at the time of operation in this series was 54 years

Nearly a third of these patients had noted their principal symptom for considerably more than a year The triad of pain, gross hematuria and renal mass is the most customary complaint, with pain uniformly present and repeatedly mentioned as the chief symptom rather than gross hematuria This is explained by the fact that squamous cell carcinoma is predominantly a comparatively avascular solid tumor, in those instances of gross hematuria in this study, the tumor almost invariably had a papillary component, usually of transitional cell carcinoma Furthermore, renal calculi were present in two thirds of the instances of hematuria The pain is not characteristic, although it usually occurs in the renal region The pain occasionally may be due to the coexistence of another pathologic entity, such as renal calculus, hydronephrosis or pyonephrosis pain in other instances may result from infiltration of the perirenal nerves, a favorite target for squamous cell carcinoma Once again, one is reminded of the urgency of undertaking thorough urologic investigation of pain in the renal region or of hematuria, gross or microscopic, in middle aged men if for no other reason than to expose this malignant neoplasm Bizarre and perverse epigastric, periumbilical, pelvic or general abdominal pain, particularly when associated with pyuria or hematuria, also necessitates urologic examination for the same reason If these symptoms stimulate more frequent urographic studies and if more kidneys are removed for calculous pyonephrosis greater hope will exist for better survival statistics in renal squamous cell carcinoma

The clinical diagnosis of a tumor of the renal pelvis was correctly made on only three occasions, testifying to the difficulty of this preoperative diagnosis This difficulty is accounted for by the dearth of pathognomonic symptoms or consistent roentgenographic or laboratory features Only cytologic identification of malignant squamous cells in the sediment of urine from a kidney suspected of containing a tumor offers any assurance of the presence of such a lesion

The fact that 57 per cent of the renal squamous cell carcinomas in this series were accompanied by renal calculi lends support to the belief that this association is not coincidental and that this relationship is not the same as that of calcification to hypernephroma Stones and chronic infection apparently represent the chief irritative agents responsible for the epithelial transformation and the development of squamous cell carcinoma It may be that a cellular predisposition exists to account for the production of this neoplasm in calculous pyonephrosis of one kidney, while the same environment does not create the tumor in another kidney This is one of the critical unknowns of the pathogenesis of tumors With the knowledge that squamous metaplasia or leukoplakia and the development of squamous cell carcinoma occur in other epithelial surfaces of the body as a result of the action of the same irritative factors, it appears pedantic to conceive that embryonic inclusions might be the source of heterotopic cells in the kidney

This study indicates that the transitional cell of the epithelium of the pelvis and calyces is the parent cell of both transitional cell and squamous cell carcinoma In the face of exposure to chronic irritative agents, whether they be calculi, specific carcinogens, toxic products of metabolism, bacteria, or deficiencies of hormones and vitamins, the normal biologic potentiality of this cell is modified to develop either a solid or papillary transitional cell epithelium If the agent, such as a calculus, has a pronounced action over a protracted period, resulting in repeated exfoliation of the mucosa, a more specialized protective cell will appear, creating an epidermoid surface that in turn may undergo malignant degeneration Sometimes, as in six kidneys of this study, both types of epithelium coexist in the same lesion, even in the same microscopic field Conversion from transitional to squamous epithelium can be demonstrated particularly well in some tumors Most of these dual lesions have a papillary component, however, squamous cell carcinoma on rare occasions may be entirely or in part a papillary tumor Grossly, one cannot be certain of the cellular type of any pelvic tumor that does not have a delicate pedicle

Most of the specimens reviewed disclosed some degree, usually extensive, of parenchymal and perirenal involvement As already mentioned, one of the outstanding surgical observations was the considerable perirenal edema and fixation from inflammation or extension of the tumor into the perirenal fat to involve Gerota's capsule In one exceptional specimen, with an "extrarenal" type of pelvis, a grade 3 squamous cell carcinoma had penetrated into the peripelvic tissues, sparing entirely the renal parenchyma

Heretofore, noninfiltrating squamous cell carcinomas of the renal pelvis were not known to exist However, gross and microscopic study of three tumors of this series left no doubt that invasion of the muscularis propria of the renal pelvis had not occurred The fact that the three patients with such lesions were living and free of any clinical evidence of recurrence 3 14 and 15 years respectively after operation is in conformity with such a pathologic diagnosis In addition two patients who had tumors involving the muscularis but not penetrating through the entire renal pelvic wall lived 4 and 15 years, respectively in the latter instance the cause of death was not related to the renal tumor Thus despite the pall of somber pessimism concerning longevity in such tumors this series shows a 5-year survival rate of 17 per cent and probable cure in 13 per cent of the patients

Squamous cell carcinoma is not exclusively a lesion of the renal pelvis but it may originate in the calyces as occurred in two patients and may extend into the parenchyma and through the capsule without disturbing the pelvis

It is improper to pass judgment on the efficacy of roentgen therapy on the basis of the five patients in this series who got such treatment In four of these patients, the tumors were of high-grade malignancy and were infiltrating the average postoperative survival after a variable amount of roentgen treatment was six months The patient who lived 15¾ years after nephrectomy for a grade 3 tumor infiltrating the muscle but not the tunica adventitia received 10 treatments during the immediate 2-year postoperative period and finally died of an unrelated disorder What bearing the roentgen therapy had on the length of survival is certainly debatable

When the survival rates of these 23 patients with renal squamous cell carcinoma are correlated with the grade of malignancy and with the depth of infiltration of the tumor, it appears that a more congruous relationship exists

TABLE 1 *Influence of grade of malignancy and extent of infiltration of renal squamous cell carcinoma on survival*

	Time since operation									
	Month			Years						
	1	3	6	1	2	3	4	6	14	15
Grade of malignancy	4 4 4 4 3 3	4 4 4 3 3 2	4 2	2 3	4	3*	2	3	1	3 3
Extent of infiltration†	C C C C C C C	C C C C C C C	C C	C C	C	A	B2	C	A*	A B2

* Patient living and well

† According to the Jewett classification

between the degree of infiltration and the survival rate than between the grade of malignancy and survival (see accompanying table) Although the Jewett[23] classification for tumors of the urinary bladder is not strictly applicable to tumors of the renal pelvis because of the intrarenal situation of the pelvis, this table indicates a strong correlation With one exception, all patients who had tumors infiltrating the entire thickness of the renal pelvic wall, namely type C, died within 2 years of operation All tumors of type C had vascular involvement of the renal hilus, which was not true in lesions of type A or B This study demonstrates that the over-all malignancy of squamous cell carcinoma of the kidney is predicated on the microscopic interpretation of sections of the tumor itself, the adjacent wall of the renal pelvis and the hilar vessels and nerves

SUMMARY AND CONCLUSIONS

A study was made of 23 cases of squamous cell carcinoma of the renal pelvis gleaned from a total of 175 tumors of the renal pelvis surgically treated at the Mayo Clinic during a 48-year period These 23 lesions make a total of 155 squamous cell carcinomas of the kidney reported in the literature, testifying to the rarity of this lesion

These 23 tumors occurred predominantly in men and with about equal frequency on either side The average age of the patients was 54 years

Chronic renal infection and calculi play an important etiologic role in such tumors Stones were present in 13 (57 per cent) of the patients, and leukoplakia was noted in four

Pathognomonic symptoms apparently are lacking, although pain, usually in the renal position, is consistently present Pyuria, microhematuria, an increased erythrocytic sedimentation rate and leukocytosis are likely to occur Urography ordinarily reveals a renal abnormality but does not specifically define the tumor An accurate preoperative diagnosis apparently never has been made, although it may be possible with modern cytologic studies on cells found in the urine

The lesion may coexist with transitional cell carcinoma and may be totally or in part papillary or solid It can occur independently in the calyces and invade the parenchyma, just as it may exist in the pelvis and extend without penetrating the parenchyma

Perirenal, hilar and distant dissemination occurs early, and the great majority of patients die within 2 years after operation

This series included three noninfiltrating and two partially infiltrating renal squamous cell carcinomas, the presence of these tumors was mainly responsible for a 17 per cent 5-year survival rate and a 13 per cent rate of probable cure A fairly exact relationship exists between the degree of infiltration of the renal pelvic wall by the tumor and the length of survival of the patient

Nephrectomy and partial ureterectomy should be the surgical procedure employed The value of roentgen therapy is inconclusive

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A PHASE CONTRAST STUDY OF THE MECHANISMS OF RENAL CALCIFICATION

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The role of altered mucopolysaccharides in the mechanism of renal calcification in recent years has come under intensive study by many investigators Many approaches to the problem have been pursued, all of them adding to the knowledge of the chemical background on which calcification occurs in the kidney The histochemical study of altered mucopolysaccharides in the calcifying kidney, though having its inception in the work of Rubin and Howard,[1] Sobel,[2] Miller, and others, was given special emphasis and clarity in the classic work of Roger Baker and his associates[3, 4] Baker's demonstration of mucopolysaccharide changes by means of selective staining techniques raised many questions about the calcification process which have as yet been only partially answered

In the histologic studies of the calcifying kidney thus far reported, the precise location and finer anatomic details of the deposition of calcium have been somewhat obscured by the histologic techniques used For example, in figures 1, 2 and 3 which are representative of the quality of the paraffin embedded sections of calcifying kidneys studied previously,[3, 4] it is obvious that at higher magnifications the finer details of the anatomy are lost Many histologic techniques have been developed in recent years by means of which much finer anatomic detail may be studied However, many of these new methods of tissue preparation, mounting, and illumination are not adaptable to histochemical studies The use of the electron microscope in the study of the kidney, though permitting visualization of extremely fine anatomic detail,[5, 6] precludes the study of tissue by selective staining techniques

It is the purpose of this paper to describe a method of more precisely visualizing the histochemical changes which occur in renal calcification No originality is claimed for the techniques used in this study The methods of tissue preparation, fixation, and staining are well established, and the use of the phase contrast

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[1] Rubin P S and Howard J E Histochemical studies in the role of acid mucopolysaccharides in calcifiability and calcification Trans 2nd Jos Macy Conf Metab 1950

[2] Sylven B J Bone & Joint Surg 29 745 1947

[3] Baker R Reaven G and Sawyer J Ground substance and calcification J Urol 71 511 1954

[4] Baker R and Sison F Demonstration of altered tissue mucopolysaccharides in renal calculous disease by selective staining techniques J Urol 72 1032 1954

[5] Pease D Fine structures of the kidney seen by electron microscopy J Histochemistry and Cytochemistry 3 295 1955

[6] Mueller C B Mason A D and Stout D Anatomy of the glomerulus Am J Med 18 267 1955

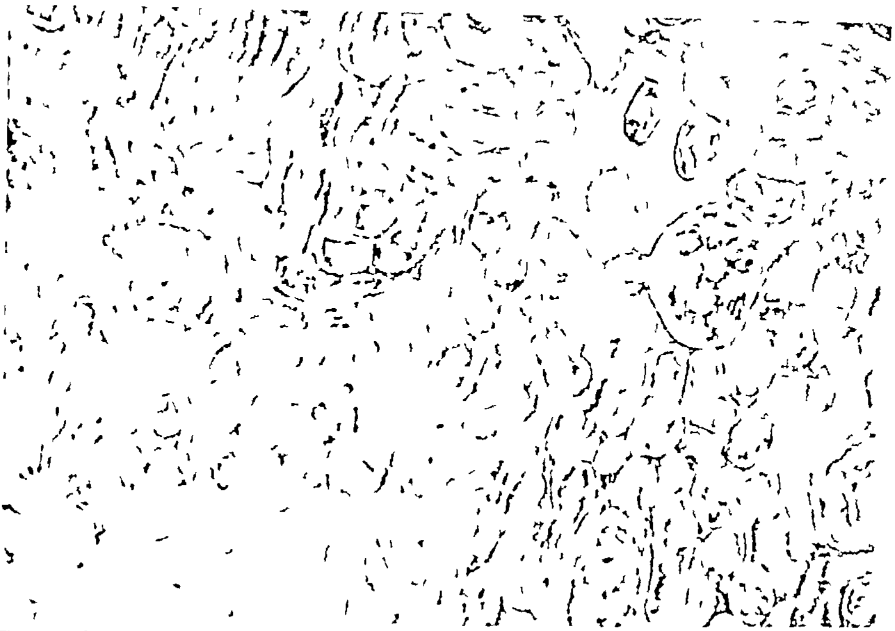

FIG 1 Normal rat kidney PAS stain, paraffin embedded tissue, transmitted light × 137

microscope in the study of renal changes is not new However, no phase study of renal calcification and the histochemical changes occurring therein have been reported

Churg and Grishman in 1952 successfully studied glomerular deposits of hyaline substances by means of the phase microscope[7] The tissue studied was prepared by the conventional paraffin embedding methods and sectioned at a thickness of two microns However, even with meticulous histologic technique, the phase contrast study of paraffin embedded tissues suffers from cellular overlap, basement membrane thickness, and loss of fine detail However, by means of plastic embedding techniques, ultrathin sectioning of tissues is possible without distortion of the architecture These methods of tissue preparation, developed for use with the electron microscope, permit satisfactory phase study of histochemically[8] stained tissues at thicknesses varying from 0 3 to 1 0 microns A number of advantages accrue from preparation of the tissue in the manner to be described It is possible to apply only one stain to a slide and yet adequately see the surrounding unstained tissue as a result of the phase contrast effect This elimination of counterstains results in less distortion Occasionally it is also of advantage to demonstrate only the one structure stained without visualization of the surrounding tissue This is possible by viewing these thin sections by transmitted light (fig 11, *A*) Thin sections also make possible a number of serial sections through a given structure, such as a glomerulus or a tubule

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[7] Churg, J and Grishman, E Phase microscopic studies of renal glomeruli Am J Path, **29** 199, 1953

[8] Houck, C E and Dempsey, E W Cytological staining procedures applicable to methacrylate embedded tissues Stain Technol **29** 207 1954

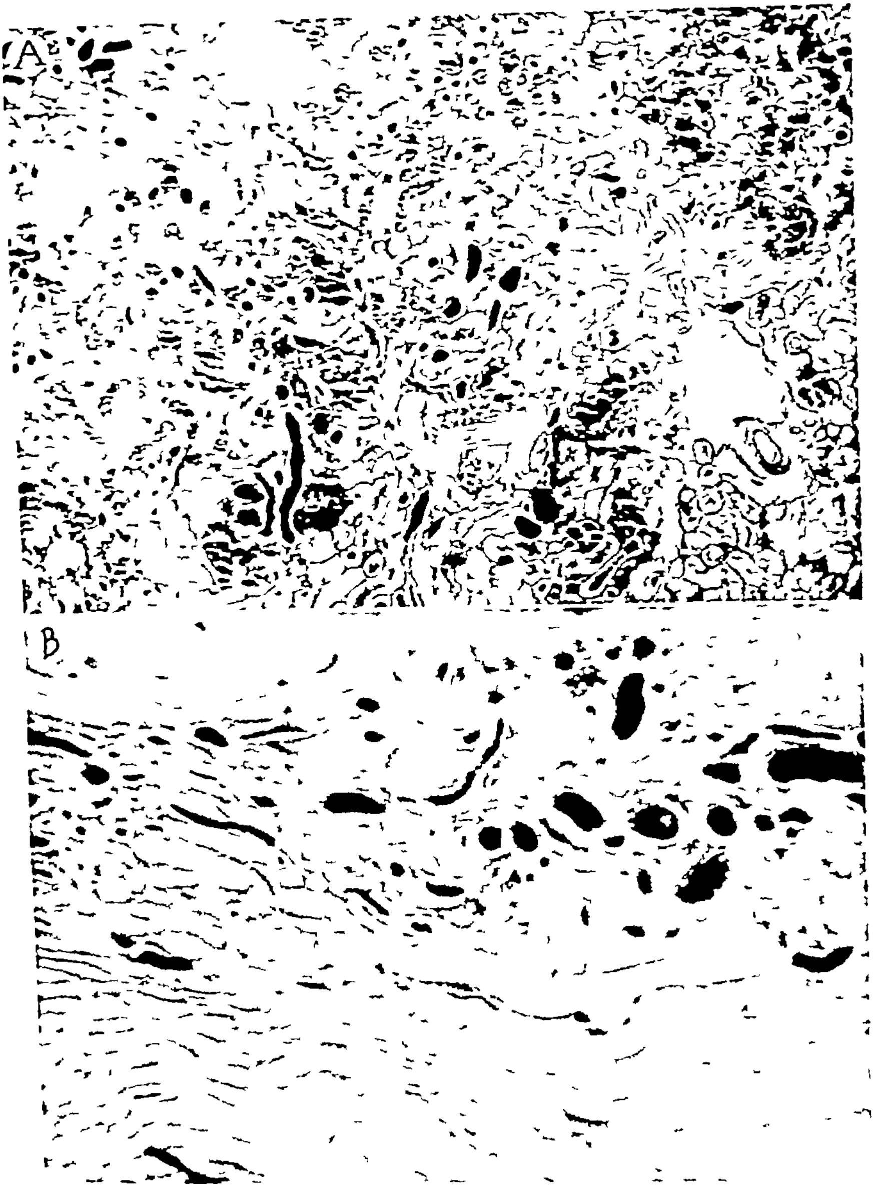

FIG. 2. A, rat kidney with parathormone induced calcification showing extensive tubule cast and basement membrane change. PAS stain, paraffin embedded tissue × 91. *B*, kidney of rat receiving 1600 units of parathyroid extract demonstrating tubules filled with material staining with periodic acid Schiff reagent. Paraffin section × 120.

METHODS

Fresh tissue sections one cubic millimeter in size were cut from the kidneys of rats maintained on regimens to be described later. These sections were immediately immersed in 1 per cent osmic acid buffered to a pH of 7.2 with Dalton's

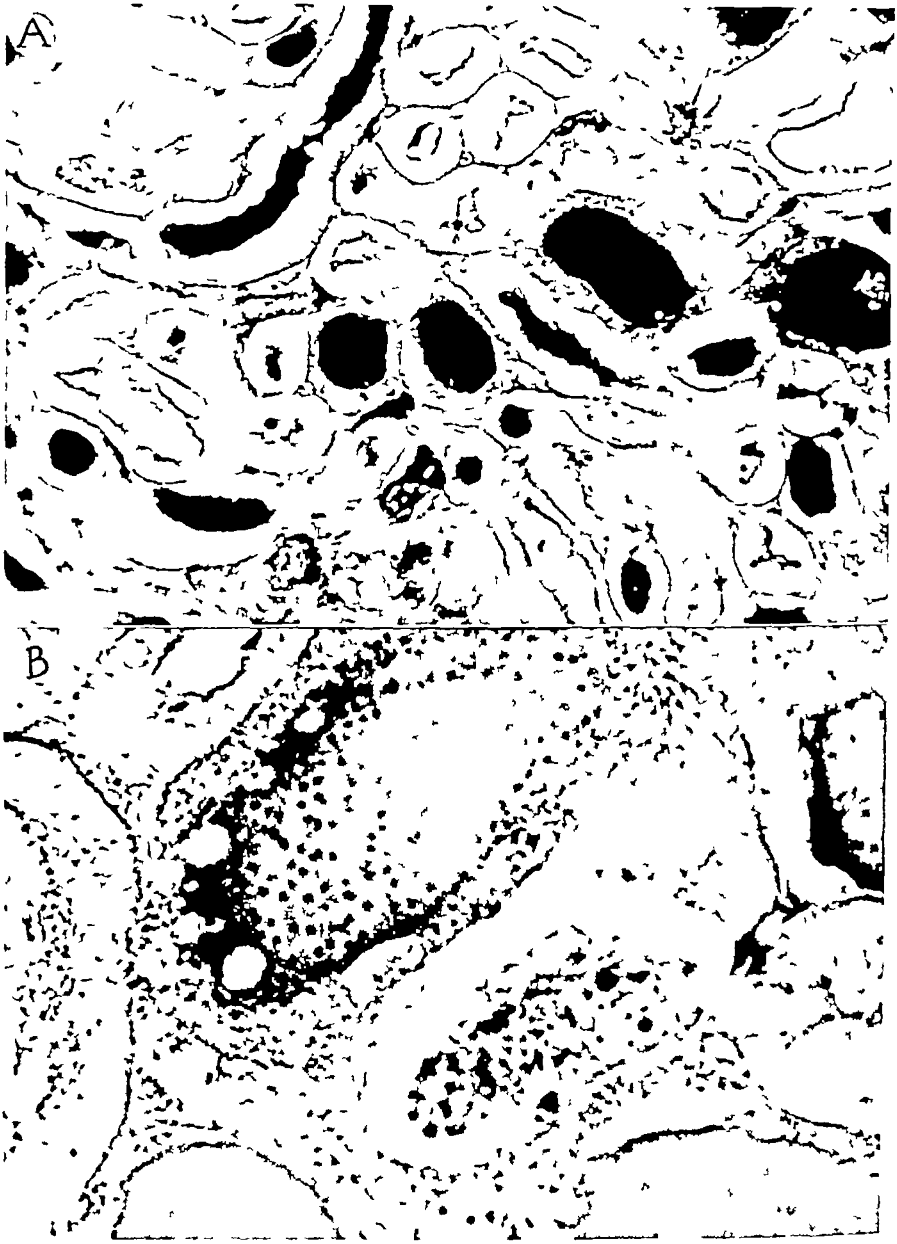

FIG 3 *A*, same as figure 2, *B* × 231 *B*, same as figure 2, *B* At this magnification it is obvious that all cellular detail is lost in paraffin sections × 1020

potassium dichromate buffer After fixation for two hours, the tissue was rinsed in three changes of distilled water and dehydrated in graded alcohols over a period of three hours as suggested by Palade[9] When dehydration was accomplished, the tissue was infiltrated with a mixture of 1 3 methyl butyl methacrylate The tissue was then embedded in No 3 gelatin capsules half filled with methacrylate to which benzoyl peroxide had been added as a catalyst After incubation at 45°C for 24 hours, the capsules were dissolved in water leaving the hard plastic slug containing the cube of tissue Sections were cut at 0 3 to 1 0 micron thickness on a Minot International rotary microtome with a glass knife[10] The sections were mounted on an albuminized microscope slide by transfer of the tissue to a drop of 50 per cent acetone with a jeweler's forceps and heat evaporation of the acetone

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[9] Palade, G E , quoted in Rinehart, J F A M A Arch Path , 59 439, 1955

Serial sections were cut from each block and dealt with in the following ways The thinner sections (0 3 to 0 5 micron) were immersed in xylol to remove the plastic and mounted unstained in paragon frozen section mounting medium Much is written regarding mounting media for phase microscopy[11] but this readily available material (paragon) gave adequate contrast with our sections and, in addition, is water soluble and semi-permanent The optimum tissue thickness for unstained sections was found to be around 0 5 micron The thicker serial sections, after removal of the plastic with xylol, were stained with the three methods described by Baker and Sison[4] Dempsey[5] showed that plastic embedded tissues could be stained almost as readily as paraffin embedded tissues Very little alteration in conventional techniques was necessary to adequately stain these sections The three stains used and their purposes were the von Kossa silver stain to demonstrate calcium deposits in the form of phosphates and carbonates,[12] the periodic acid-Schiff reaction to demonstrate compounds containing a glycol linkage such as mucopolysaccharides,[13] [14] [15] and a combination of the two as suggested by Sison,[4] in order to show deposition of calcium in the areas of altered mucopolysaccharides

In addition to the above method of tissue preparation, sections from each of the kidneys studied were fixed in 10 per cent formalin, embedded in paraffin and sectioned on a conventional microtome These slides were then stained in each of the three described manners The purpose in this was to show that the same tissue changes as previously described by others were being produced and studied except in greater detail All the animals used in this study were young adult albino male rats of the Sprague-Dawley strain weighing from 150 to 300 grams Since there was no intention of determining quantitatively the incidence of renal calcification in rats under the conditions of the experiment, the number of animals used was only large enough to insure production of the desired lesions All the animals were maintained on a standard laboratory chow and given water ad lib

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[10] Dempsey E W and Lansing A I Improved knife holders for sectioning with rotary microtomes Proc Soc Exp Biol and Med, 82 253, 1953

[11] Bennett A H Jupnik Helen Osterberg H and Richards O W Phase Microscopy Principles and Applications New York John Wiley & Sons, Inc 1951 pp 172-180

[1] Cited in Glick D Techniques of Histo and Cytochemistry New York Interscience Publishers Inc 1949 p 17

[13] Hotchkiss P D A microchemical reaction resulting in the staining of polysaccharide structures in fixed tissue preparations Arch Biochem 16 131 1948

[14] McManus J F A The periodic acid routine applied to the kidney Am J Path, 24 643 1948

[15] McManus J F A Uses of periodic acid Stain Technol 23 199, 1945

Calcific changes were produced by the same methods which Baker followed

1) *Parathormone group* Forty rats were given parathyroid extract* by the method of Chown[16] over a two-week period and all of them sacrificed on the fourteenth day Ten rats were given 1000 units of parathormone, 10 rats were given 1600 units of parathormone, 10 rats were given 1000 units of parathormone and daily intraperitoneal injections of 3 ml of a 0 04 per cent solution of toluidine blue, 10 rats were given 1600 units of parathormone and daily intraperitoneal injections of 1 5 mg desoxycorticosterone acetate

2) *Oxamide group* Oxamide was administered in the food in the amount of one to two grams per day to each of 10 rats for five days and the animals sacrificed on the seventh day

3) *Uric acid group* Uric acid was administered in the food to two groups of rats five rats were fed one gram per day for 12 days and sacrificed, five rats were fed one gram daily for 21 days and sacrificed

Five rats were fed on the standard laboratory chow and received no medications These were sacrificed on the fourteenth day for use as controls Five rats were given daily intraperitoneal injections of 1 5 mg DOCA† or two weeks Five rats were given daily intraperitoneal injections of 3 ml of a 0 04 per cent solution of toluidine blue for two weeks Five rats were given daily intraperitoneal injections of 1 5 ml of 10 per cent calcium gluconate for 14 days Although no serum calcium determinations were made, each of these rats received a total of 2100 mg calcium gluconate Inasmuch as a dose of 1775 mg over a period of 28 days is known to produce a mean serum calcium elevation of 1 9 mg per cent or to the same level as the hypercalcemia resulting from parathormone administration, this is assumed to be more than an adequate amount to ensure hypercalcemia

RESULTS

On autopsy, less calcification was found in the kidneys of the rats receiving 1000 units of parathormone than in those receiving 1600 units, as would be expected from Baker's findings Two findings were common to all these animals receiving parathormone Many subcapsular whitish plaques were present on the surface of the kidneys, and the bladders usually contained masses of white spongy, occasionally gritty, material This latter may represent desquamated epithelium or protein matrix in the process of calcification Gross calculi were found in the renal pelves and ureters and bladders of the animals receiving 1600 units of parathormone In the rats receiving toluidine blue in addition to the parathormone, soft bladder masses were seen, there was mottling of the surface of the kidneys, and the omentum and serosa of the small bowel contained deposits of the toluidine blue material Calcification was grossly inhibited in the animals receiving DOCA in addition to the parathormone

In none of the kidneys of the animals receiving uric acid were calculi seen When no gross calculi were found after 12 days of uric acid administration, a

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* Parathyroid extract gratuitously supplied by Eli Lilly & Co , Indianapolis, 6 Ind

[16] Chown, B Parathyroid and vitamin D nephritis J Path and Bact 49 273, 1939

† Desoxycorticosterone acetate supplied by Upjohn Co , Kalamazoo, Mich

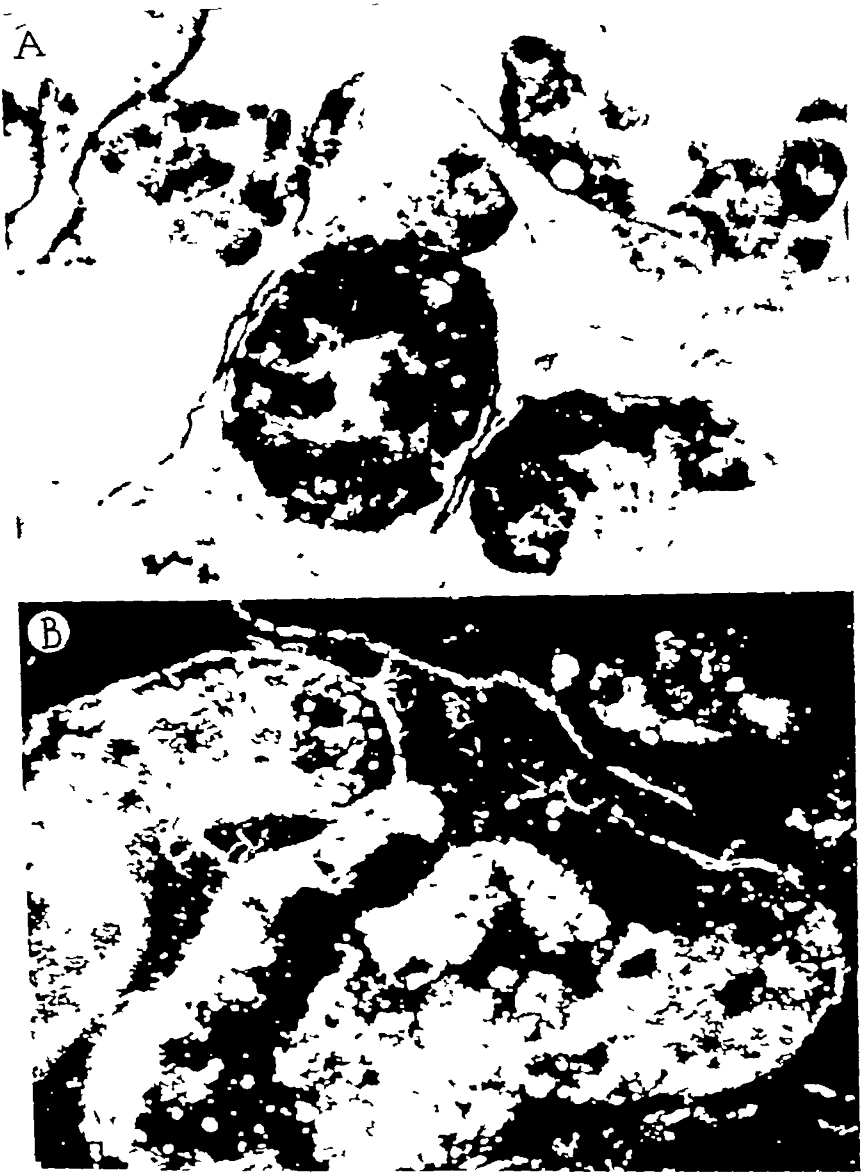

Fig 4 A rat kidney with parathormone induced calcification showing separate calcification of tubular cytoplasm in droplet form and tubular basement membranes Von Kossa stain, plastic embedded tissue, phase × 1280 *B* rat kidney with parathormone induced calcification demonstrating droplet nature of intracytoplasmic calcification with breakdown of cell membranes and calcification of tubule basement membranes Von Kossa stain, plastic embedded tissue, darkfield illumination × 1020

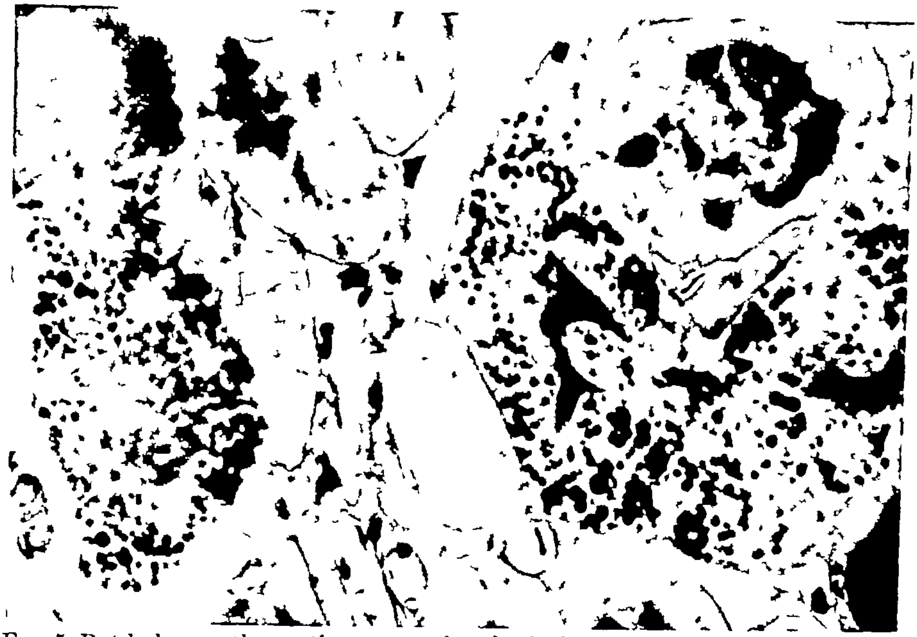

FIG 5 Rat kidney with parathormone induced calcification showing calcium deposition in intracytoplasmic droplets with failure of calcification of PAS positive casts in tubule lumen Sison stain, plastic embedded tissue, phase X 1020

second group of rats was given uric acid for nine more days but still without the production of calculi The kidneys of the animals receiving 12 days of uric acid were normal on gross examination In the remainder of the group, the kidneys were pale and mottled with occasional infarcts In three of these latter rats large whitish bladder masses were found

A greater amount of calcification was present on gross examination in the rats receiving oxamide than in any other group A number of these animals had multiple calculi in the renal collecting systems with gross hydronephrosis or pyonephrosis proximal to the stone

Of the animals receiving intraperitoneal calcium gluconate, one died after 10 days of injections At postmortem examination he was found to have obstruction of the terminal ileum with perforation of the small bowel just proximal to that point Another animal was moribund when sacrificed and was found to have obstruction at the ileocecal valve with necrosis of the terminal ileum No gross calculi were seen but the surface of the kidneys appeared mottled and the bladders contained white spongy material

Examination of the paraffin sections disclosed consistent changes which directly paralleled those found by Baker The patchy increases in the PAS positive material of the tubule cytoplasm and basement membranes, and lumens, were noted especially in the corticomedullary areas, which have been interpreted as increase in depolymerized mucopolysaccharides (figs 2 and 3) The examination of the thin sections with the phase microscope revealed many additional facts about these kidneys In general, the following features characterized the phase

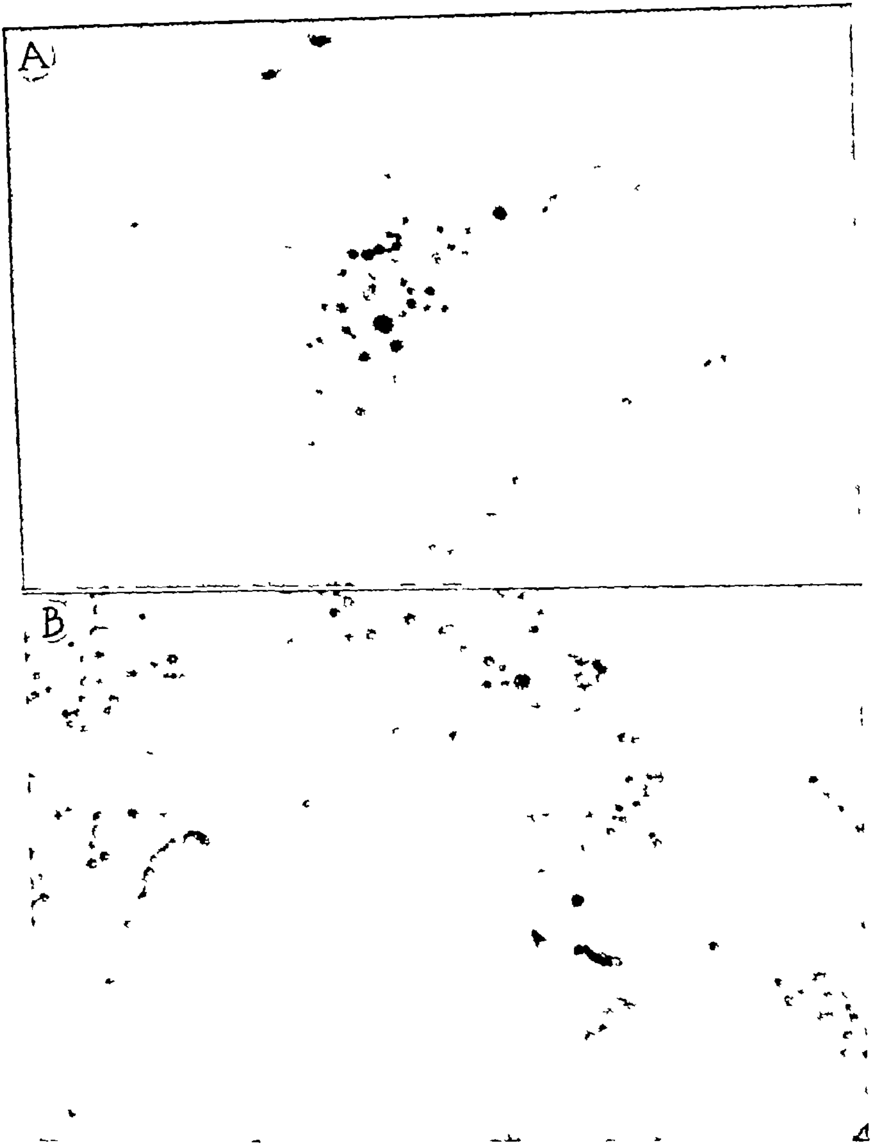

Fig 6 *A*, parathormone induced calcification in rat kidney showing droplet formation in cytoplasm of tubular epithelium PAS stain, plastic embedded tissue, phase × 1280 *B*, same as *A* Phase illumination, no stain Note associated vacuolization of tubular cells and absence of mitochondria × 1160

study of the thin sections Intracytoplasmic cellular detail became clearly visible, at higher magnifications, the mitochondrial rodlets could easily be distinguished (fig 9, *B*), brush borders could be seen, juxtaglomerular apparatus was visible (fig 9, *A*), and certain fine cellular changes became manifest

Parathormone group In the kidneys of the rats receiving parathormone, three

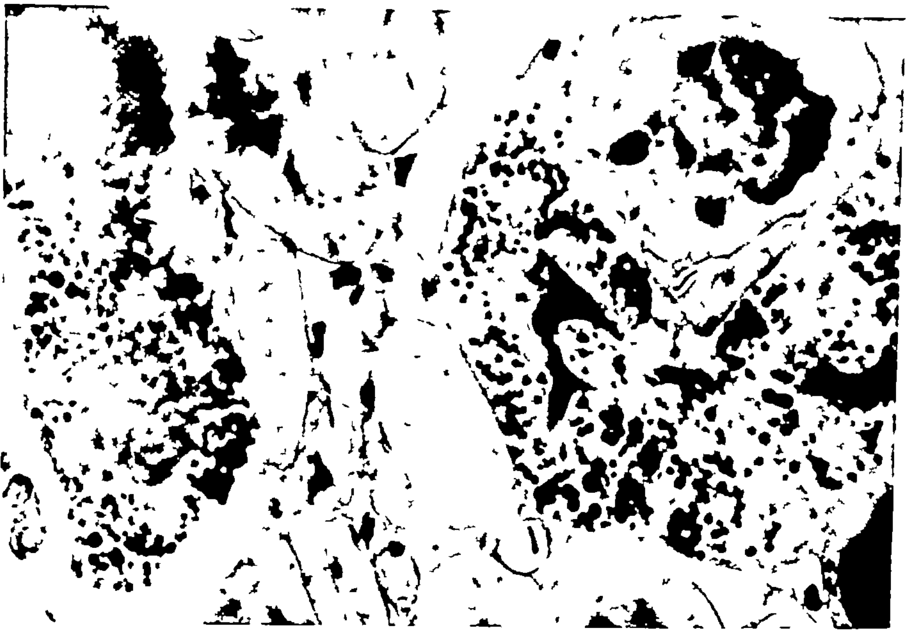

FIG 5 Rat kidney with parathormone induced calcification showing calcium deposition in intracytoplasmic droplets with failure of calcification of PAS positive casts in tubule lumen Sison stain, plastic embedded tissue, phase × 1020

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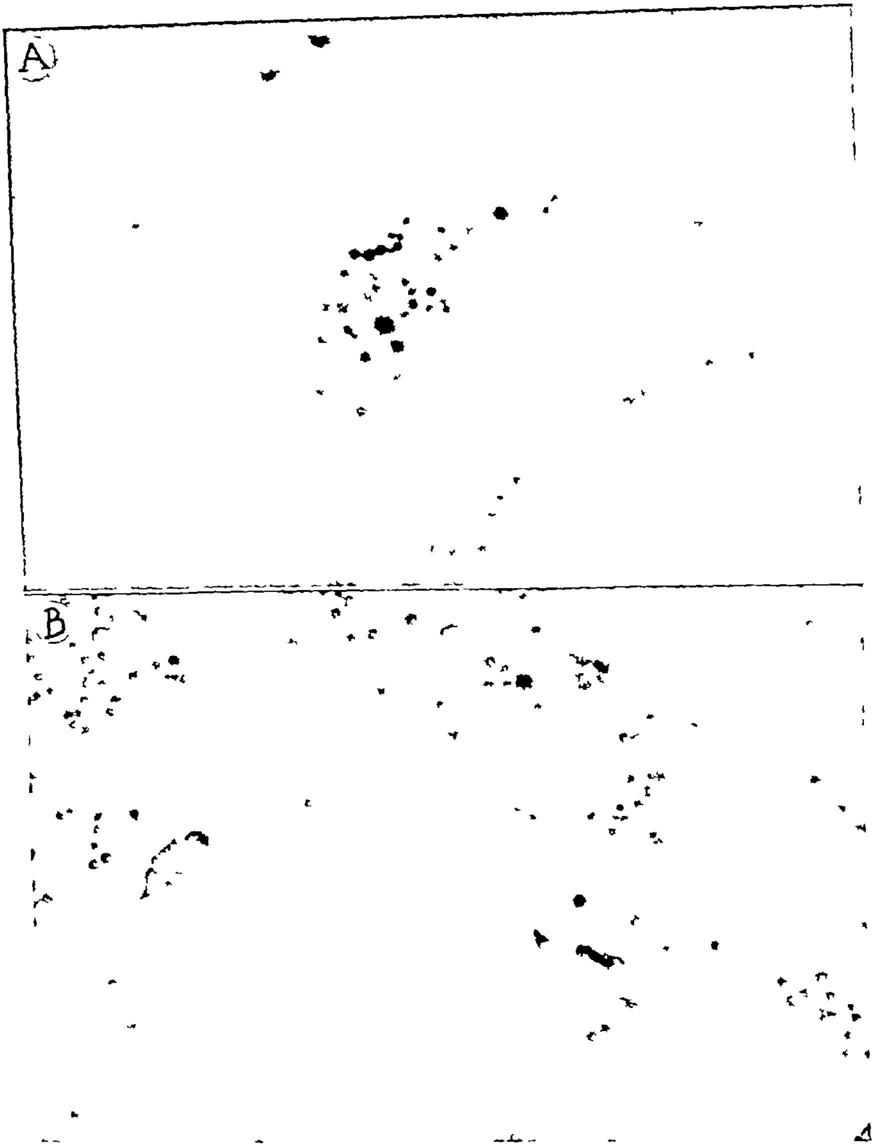

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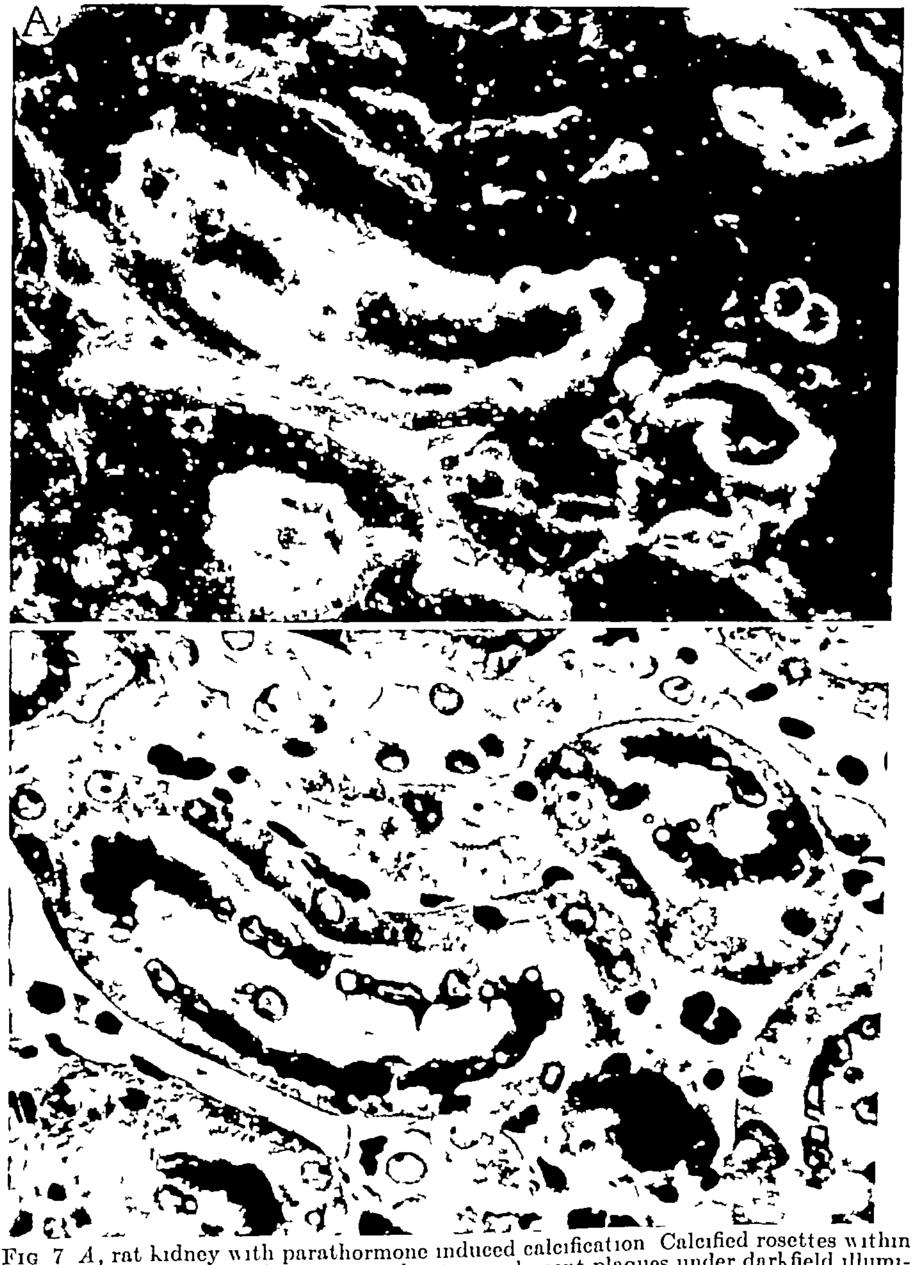


Fig 7 *A*, rat kidney with parathormone induced calcification Calcified rosettes within lumen of tubules—calcium deposits stand out as iridescent plaques under darkfield illumination Von Kossa stain, plastic embedded tissue × 1020 *B*, same as *A*, but with phase illumination Tubular cells near calcified rosettes are relatively uninvolved in calcifying process × 1020

distinct changes can be noted 1) On the PAS stains, the basement membranes of tubules containing calcium are thickened This manifests itself in two ways these basement membranes stain more heavily than in surrounding uninvolved tubules, but also the basement membrane, by virtue of its thickening, assumes a fibrillar appearance (fig 9, *B*) Although this fibrillar appearance may be artefact it is seen consistently in these sections and suggests a true spiral fibrillar nature to the tubule basement membrane The von Kossa stain shows clearly the basement membrane calcification (fig 4) 2) The second change noted is that on the

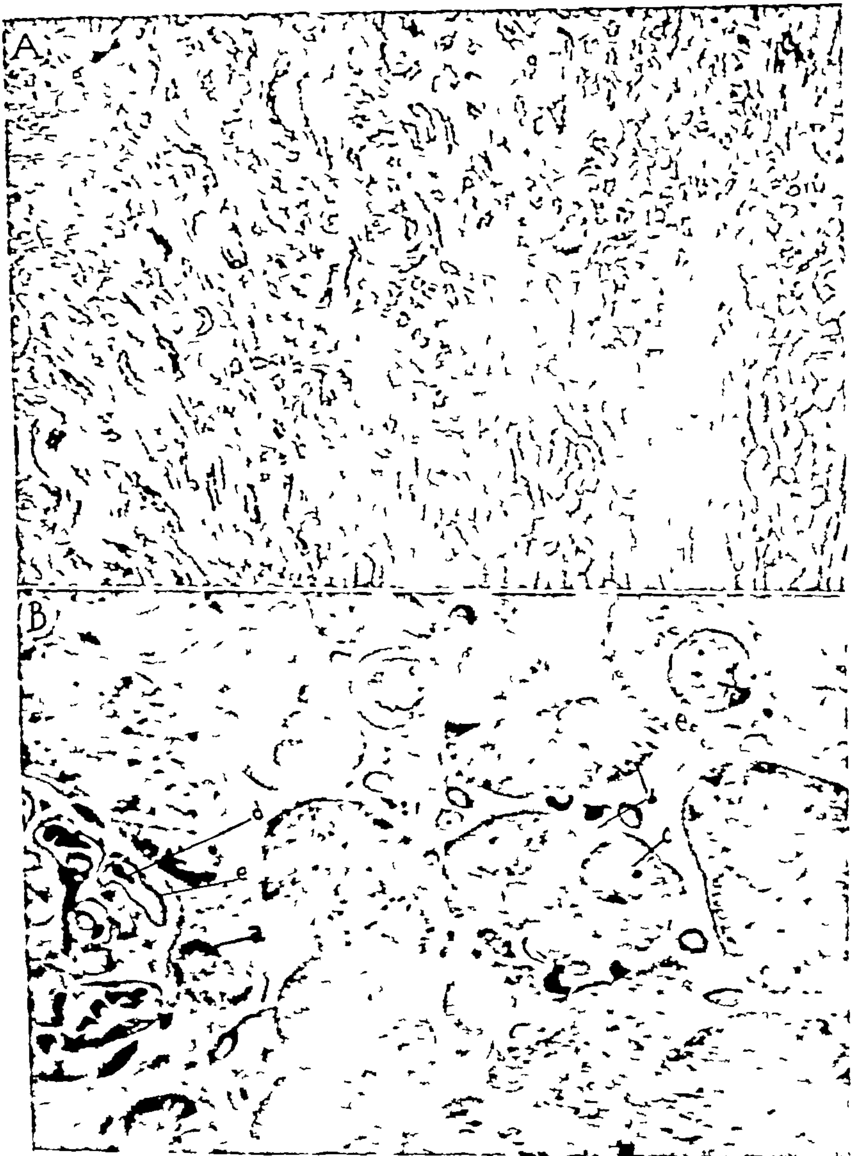
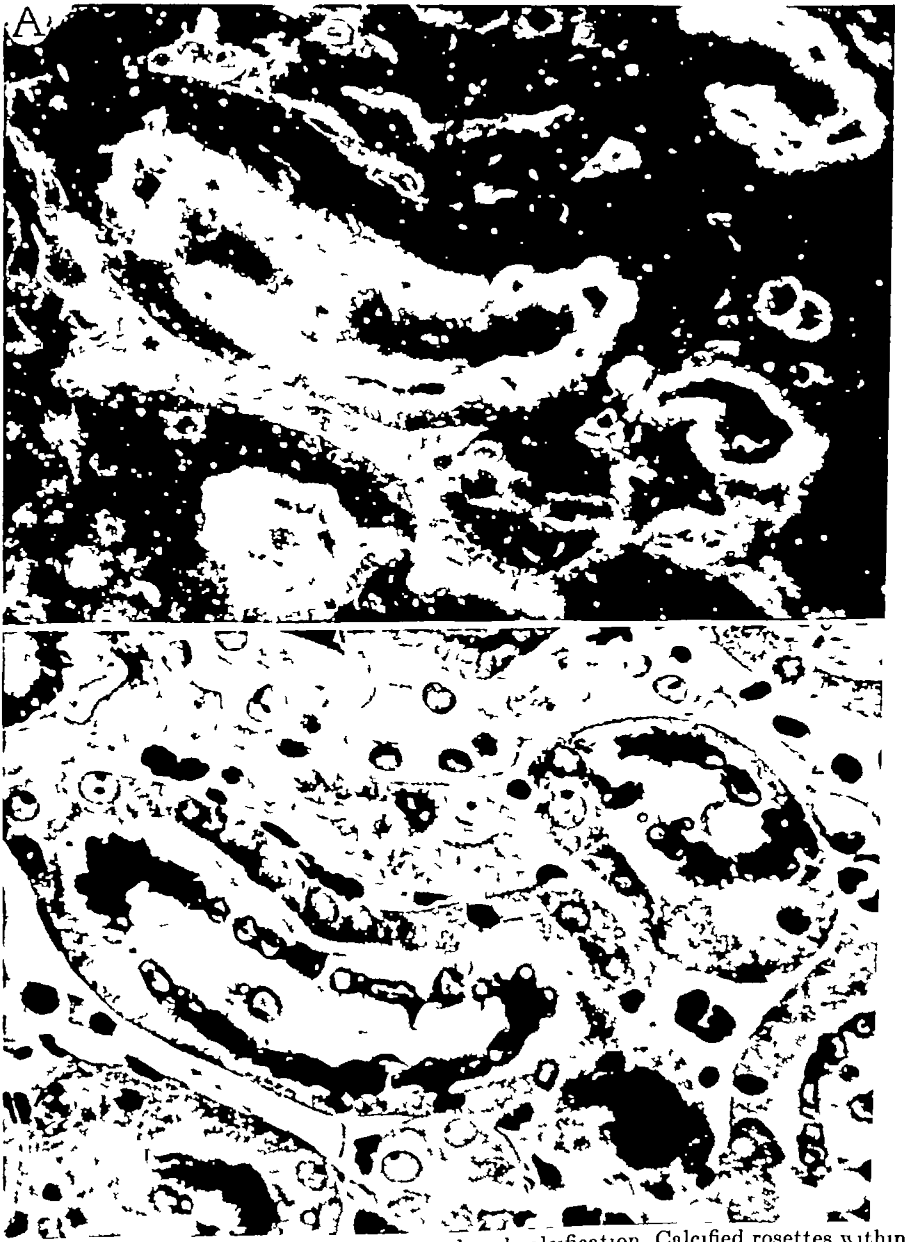


Fig 8 A, rat kidney Renal changes coincident with uric acid ingestion PAS stain, paraffin embedded tissue × 89 *B*, kidney of rat receiving uric acid Anatomic detail visible *a*) juxtaglomerular apparatus *b*) mitochondria *c*) nuclei and their nucleoli *d*) red blood cells *e*) glomerular capillary Vacuolization of proximal tubules may be secondary to osmic fixation Unstained plastic embedded tissue phase × 1020



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All stages of this intradroplet calcification can be seen, some of the droplets being hardly calcified, and others heavily so It is noteworthy that only proximal convoluted tubules are ever seen to be involved in this process of droplet calcification, and not all the proximal tubules in any given area are affected In many

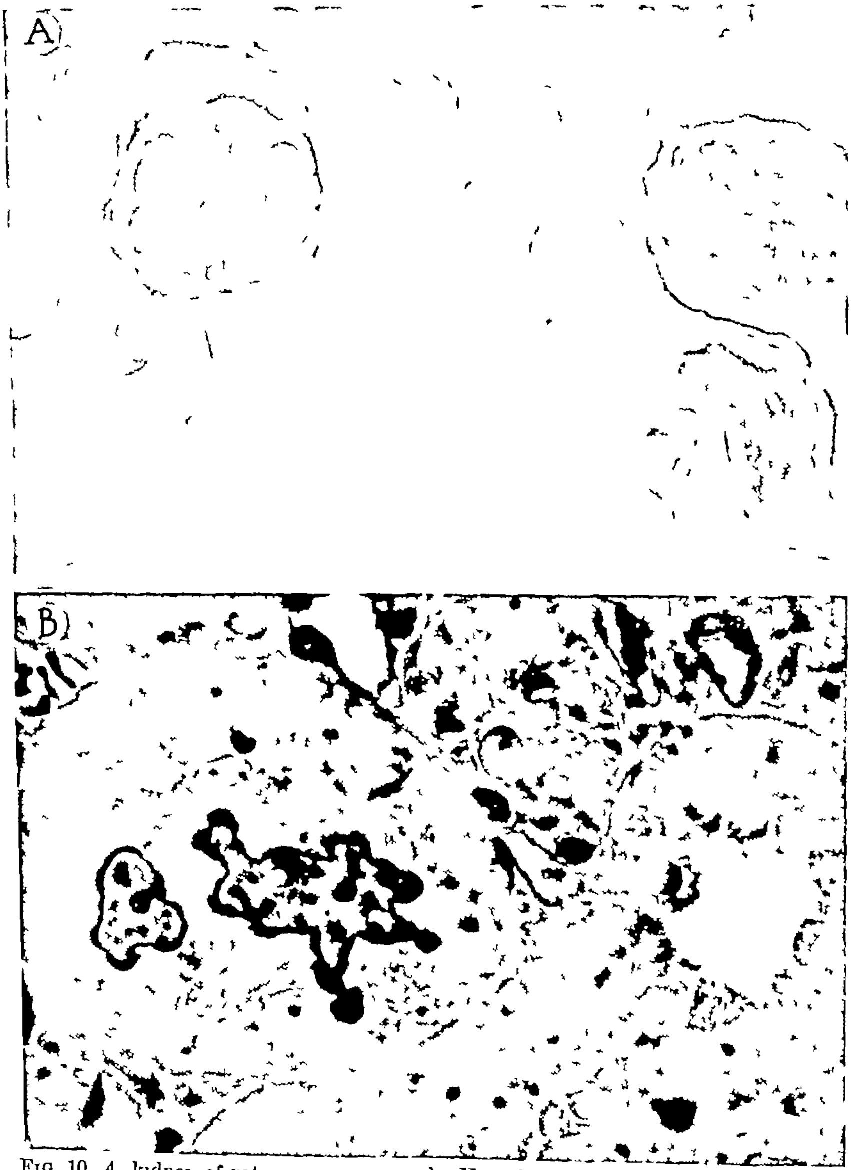

FIG 10 *A*, kidney of rat receiving oxamide Heavily staining material in lumen of tubules PAS stain, paraffin section × 380 *B*, kidney of rat receiving oxamide Large calcific plaques in tubule and no significant alteration of tubule epithelium architecture Von Kossa stain, plastic embedded tissue, phase × 1300

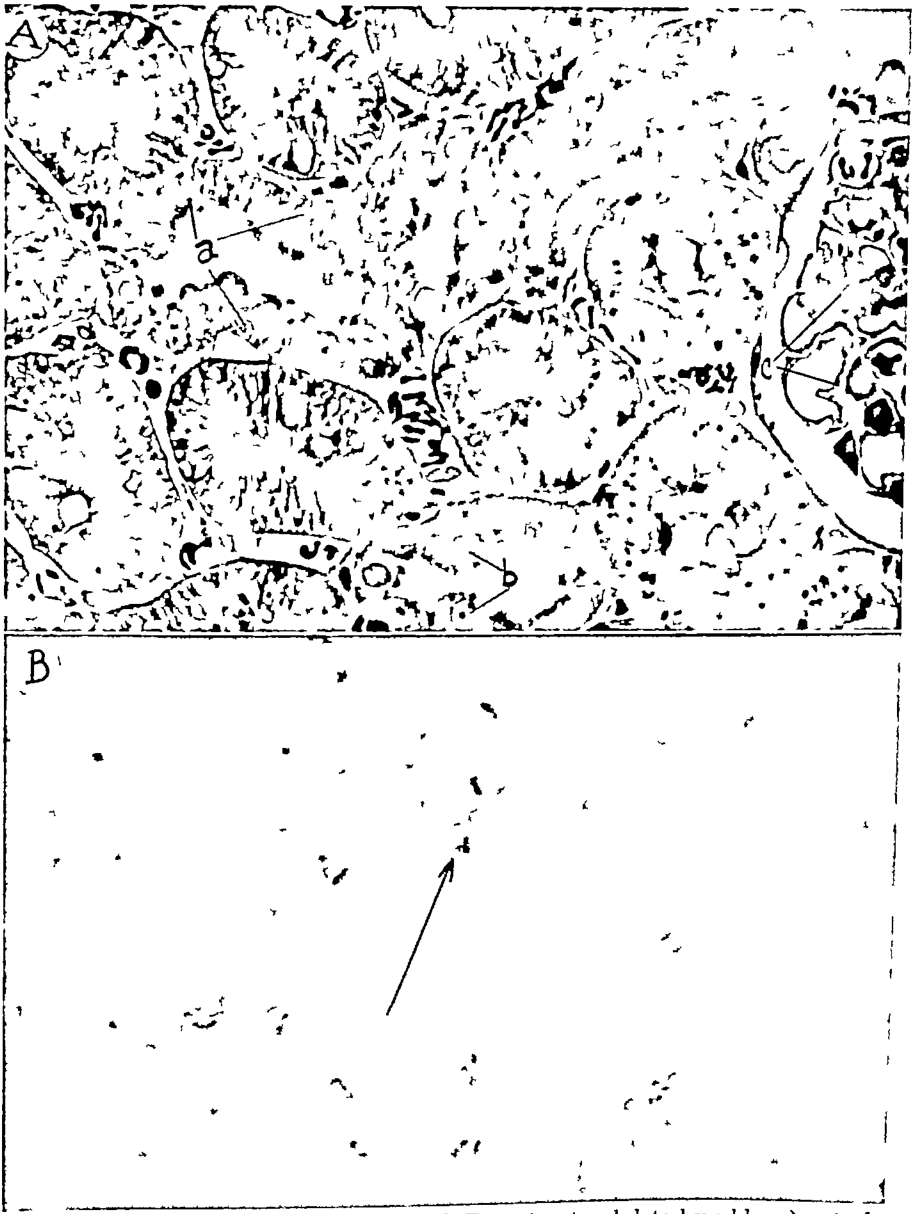

FIG 9 *A*, kidney of rat receiving uric acid Fine structural detail visible, *a*) mitochondria, *b*) nuclei and their nucleoli, *c*) intercapillary podocytes in glomerulus Proximal tubular droplets are much smaller than in parathormone group Unstained plastic embedded tissue phase × 850 *B*, kidney of rat receiving uric acid Tangential cut of tubule reveals spiral fibrillar nature of basement membrane PAS stain, plastic embedded tissue, phase × 850

von Kossa stained sections virtually all the cytoplasmic calcification has a globular or droplet form (figs 4, *B*, 5 and 6, *B*) A serial section bearing a PAS stain shows these droplets to be strongly PAS positive (fig 6, *A*), and a Sison stain shows that calcification is occurring within these PAS positive droplets (fig 5)

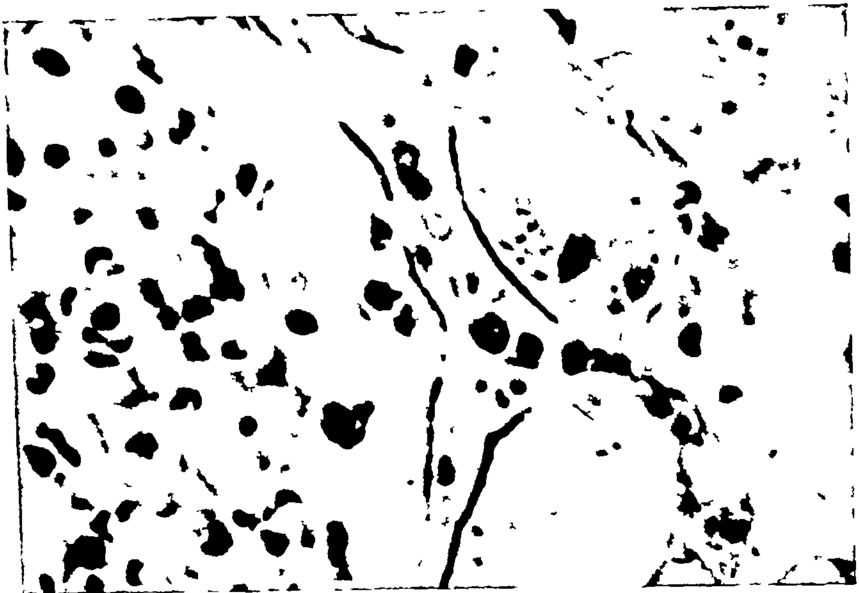

FIG 12 Rat kidney containing calcification induced by administration of calcium gluconate Calcium is being deposited in parietal layer of Bowman's capsule as well as in basement membranes of tubules Von Kossa stain plastic embedded tissue, phase × 1020

droplet calcification while an adjacent part of the tubule was relatively normal The patchy calcification always seemed to involve groups of adjacent tubules seldom single tubules In extensively calcified tubules the architecture of the cells was destroyed with entire tubules becoming little more than a mass of calcified and calcifying granules or droplets (fig 4 *B*) In other areas PAS positive casts can be seen filling tubule lumens (figs 2, 3 and 5)

The third change seen in the group receiving parathormone was the presence of rosettes of calcification filling certain tubule lumens, usually distal tubules This rosette is thought to be composed of droplets which have calcified higher in the tubule and moved downward inasmuch as the cytoplasm of adjacent tubular cells is relatively uninvolved Figure 7 *A* shows the calcium rosette within the lumen of the tubule Figure 7, *B* shows the normal cells lining the tubule at this point

Phase contrast study of unstained serial sections of the slides mentioned above reveals further information about the changes in rats receiving parathormone The mitochondrial rodlets normally clearly visible in normal tubules (fig 8) are seen to be either in the process of alteration into droplets or have disappeared entirely (figs 5 and 6) in the calcifying tubules as noted by J Oliver[17] There appears to be more vacuolization of the cytoplasm of involved tubules than seen in normal tubules When one area of a tubule is undergoing calcification the mitochondrial rodlets in nearby portions of the same tubule are not normal either being scattered away from their usual orderly location as a "picket fence" arrangement along the base of the tubular cell, or actually visible changing from

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[17] Oliver J, McDowell M and Lee J C J Exp Med 99 589 1954

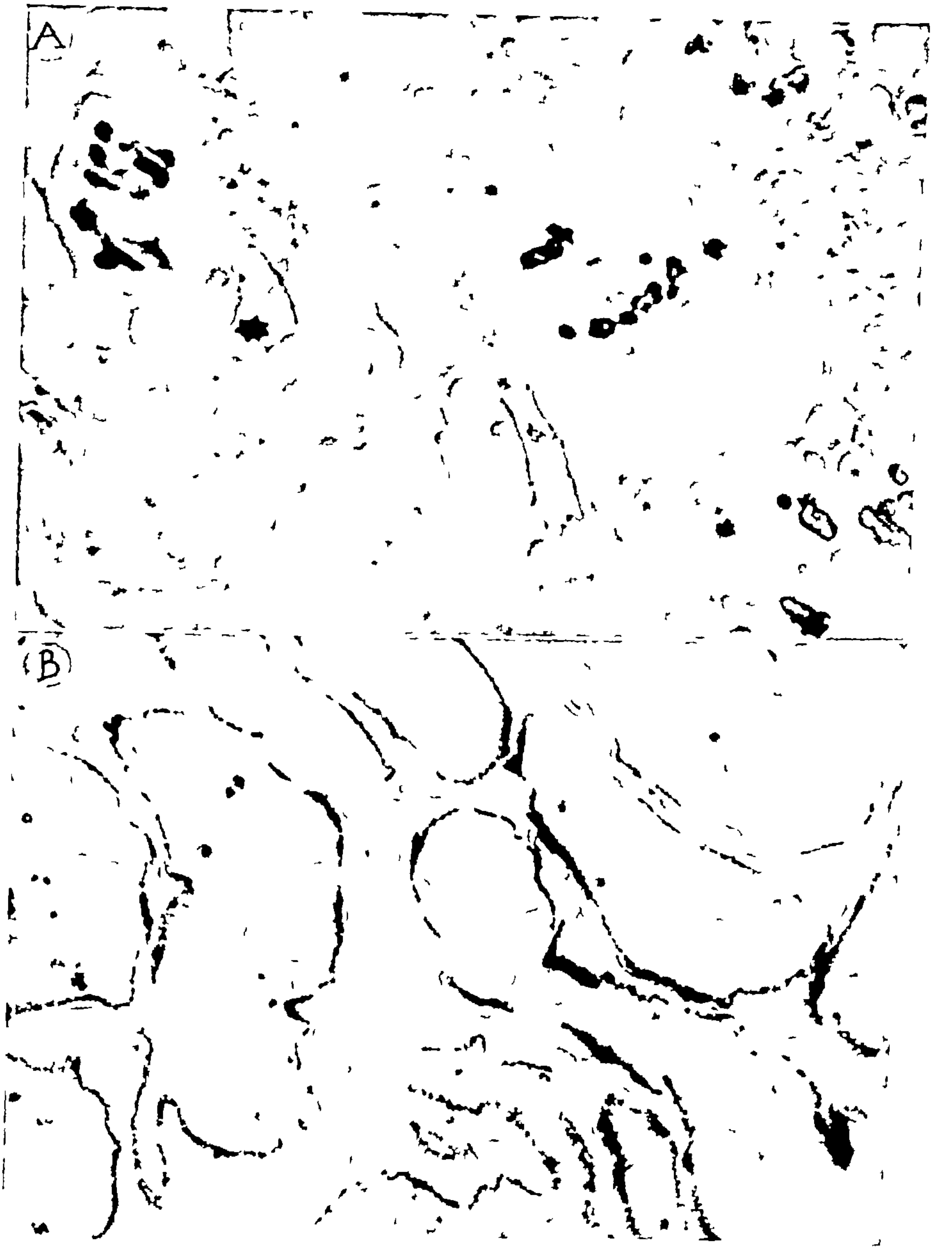

FIG 11 *A*, kidney of rat receiving oxamide showing calcific tubular epithelial plaques Von Kossa stain, phase × 1050 *B*, rat kidney with calcification induced by calcium gluconate administration showing basement membrane calcification Von Kossa stain, plastic embedded tissue, transmitted light × 910

of these there appears to be separation of the cytoplasm of the cell from the tubular basement membrane with separate calcification of the basilar membrane of the tubular cell (fig 4, *B*) although this may be an artefact of osmic fixation or thin sectioning In some tubules, one portion was extensively involved in the in the kidneys The paraffin sections revealed minimal but definite increase in the PAS positive material in the tubules of the corticomedullary junction area (fig 8, *A*) No uric acid crystals were ever identified Phase study of the thin sections revealed some increased vacuolization of proximal tubular cells, some increase in PAS positive granules, and some thickening of the basement membranes, as evidenced by the increased fibrillar appearance (figs 8, *B* and 9)

Not as many granules or droplets were noted as in the parathormone group and there was less vacuolization of the proximal tubular cells As would be expected, no calcium depositions were noted

Oxamide group Paraffin sections of the kidneys of the rats fed oral oxamide revealed two consistent changes In many of the tubules were crescent shaped plaques of strongly PAS positive material (fig 10, *A*) The nature of this material is not known, but it may be inspissated protein as a result of the extensive tubule dilatation secondary to the hydronephrosis which was quite marked in most of the kidneys of this group There were also seen numerous areas of calcific change in the dilated, scarred, chronically damaged tubules Phase study of the thin sections revealed many intracytoplasmic calcific plaques which bear no resemblance to the intracytoplasmic calcification in the parathormone group These placques appear to have resulted from the coalescence of more than one calcific focus (figs 10, *B* and 11, *A*) The tubular cells show some vacuolization, with disturbance of the rodlets, and minimal droplet formation

In the kidneys of the animals receiving intraperitoneal calcium gluconate, the findings were remarkable There were seen areas of definite tubular basement membrane calcification with no cytoplasmic calcification (fig 11, *B*) and also calcification of the basement membrane of the glomerulus which comprises the parietal layer of Bowman's capsule (fig 12) both of which findings are reported to never occur[4, 5] The same slide which shows the calcific tubular basement membranes (fig 11, *B*), when viewed with phase, reveals extensive vacuolization of the cells of the tubules involved, these being always proximal convoluted tubules (fig 13, *A*)

DISCUSSION

The many investigative approaches to the problem of the histochemical background of renal calcification have led to the conclusion that altered ground substance or derivatives thereof are somehow involved in the calcifying mechanisms Ground substance is known to contain, among other things, mucopolysaccharides These substances are polysaccharides containing amino sugar and uronic acid units as a part of their structure The name, mucopolysaccharide is derived from the fact that some of these compounds are found in mucus secretions[18] Mammalian mucopolysaccharides may be divided into two groups those formed by mucus glands and goblet cells (e g mucoitin sulfate), and those occurring in connective tissue (e.g hyaluronic acid, chondroitin sulfate, and heparin)[19] Hyaluronic acid and chondroitin sulfate, both components of the ground

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[18] White, A, Handler, P, Smith, E L and Stetten, DeW Jr Principles of Biochemistry New York McGraw-Hill, 1954, p 810

[19] Ehrich, W E In Etiologic Factors in Renal Lithiasis Springfield, Ill Charles C Thomas, 1956, p 278

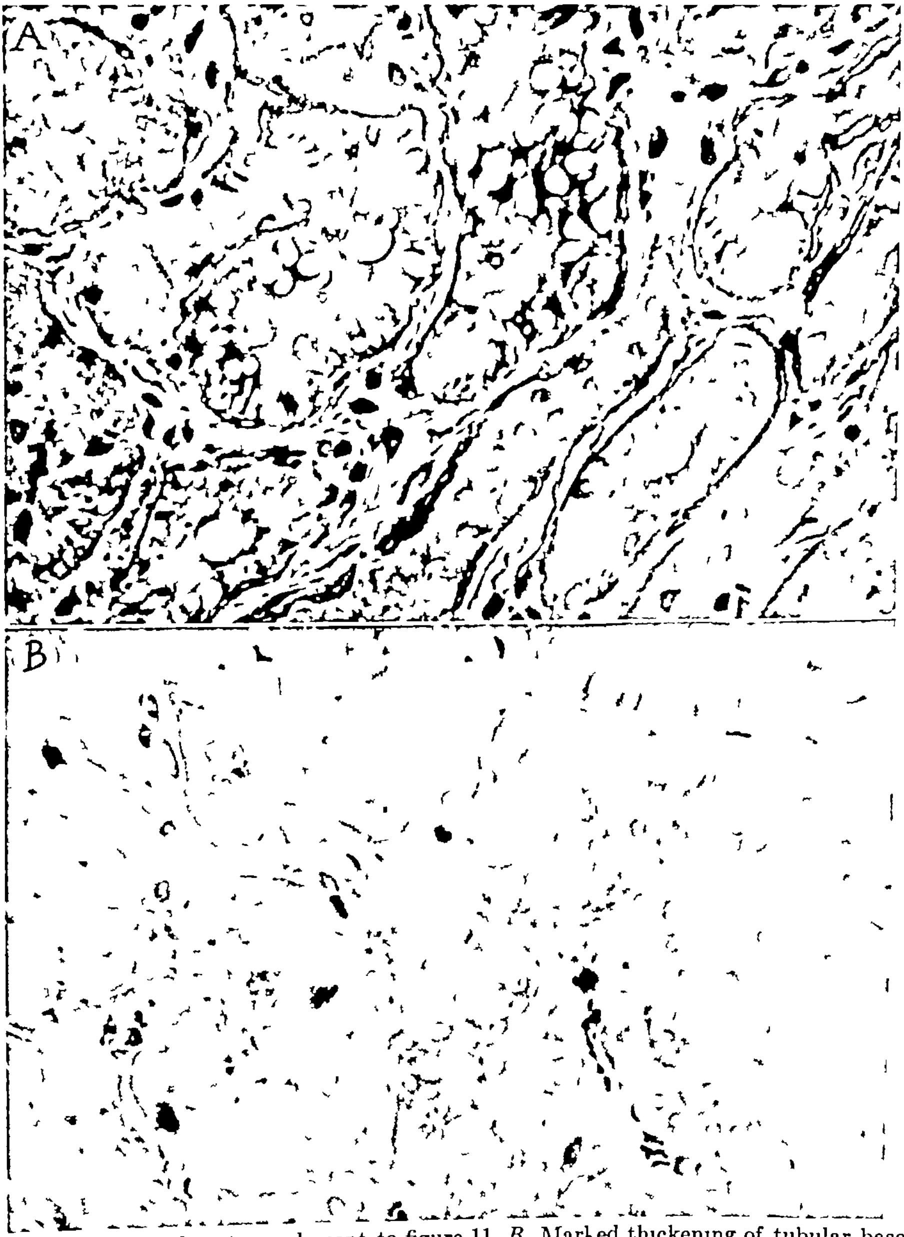

FIG 13 A, serial section adjacent to figure 11, *B* Marked thickening of tubular basement membranes with extensive vacuolization of tubular cells Unstained, plastic embedded tissue, phase × 830 *B*, rat kidney with calcium gluconate induced calcification Involved tubules show extensive epithelial damage compared with adjacent uninvolved tubules Unstained, plastic embedded tissue, phase × 930

rodlet to droplet form Changes are seen in many more tubules by phase microscopy than in the stained sections which would seem to indicate that there is a finer architectural change which precedes the grosser alterations seen with stains

Uric acid group The animals fed uric acid showed fewer microscopic changes intimately involved in the calcifying process in the kidney. Boyce has perhaps done more to establish this thesis than anyone else. He was able to dialyze a protein out of the urine of patients with calculous disease which is not found in the urine of normal subjects. This protein binds calcium when redialyzed against normal urine, and has an electrophoretic mobility different from that of any component of normal urine.[21] From the urine of normal subjects and of patients with calculous disease Boyce has also isolated a protein of large size thought to be a product of secretion by the urothelium.[22] This uromucoid, as it was called, failed to bind calcium until it was disrupted by solution in buffers of pH 12.3, whereupon smaller units were produced which were found to bind calcium. From these and other studies came the feeling that a urinary protein in order to be implicated in the calcifying mechanism must be in a disrupted or reactive state. The presence of this large uromucoid, though bearing a positive correlation to the occurrence of PAS positive granules consistently found in the transitional epithelium removed from the urinary tract of patients with calculous disease is nevertheless not proven to have any significant part in the calculous matrix.[23] Boyce suggests that keratosulfate, demonstrated in bone matrix and in the cornea by K. Meyer, may be the mucopolysaccharide substrate essential for calcification. The PAS positive mucoprotein component of calculous matrix, apparently separate from the mucopolysaccharide mentioned above, is of unknown origin.

The above discussion, though admittedly detailed, is thought essential to supply the background whereby the findings reported in this paper may be intelligently interpreted. First of all, in comparing the finer histologic changes in the kidneys of rats undergoing different types of calculus formation (parathormone, uric acid, oxamide) there is very little similarity between types. It is true that the PAS stains of paraffin embedded tissue from each group show intense PAS staining. The possibility arises that this affinity for the PAS stain does not represent depolymerized mucopolysaccharide but rather is an indication of the rigidity of the bond between the mucopolysaccharide and the protein to which it is bound. Indeed, it appears from the work of Boyce that if a mucopolysaccharide is involved in the calcifying process apart from a mucoprotein, we do not visualize it with the PAS stain, and the component seen on the PAS stain is the mucoprotein component.[23] If the PAS positive material seen in these studies of renal calcification is the mucoprotein spoken of by Boyce, then its intensity of staining could be explained on the basis of its chemical bonds, which, according to Boyce, so strongly unite this mucoprotein to its mucopolysaccharide (which stains only with toluidine blue) that separation is difficult without causing its degradation to its component monosaccharides and amino acids.

The origin of the mucoprotein may be partly explainable on the basis of the histologic structures and alterations seen on the thin tissue sections of this study. It appears that there are two facets to the calcification noted in the parathormone group. The droplet formation and the intraluminal calcification are probably the

[21] Boyce, W. H., Garvey, F. K., and Norfleet, C. M.: Proteins and other biocolloids of urine in health and calculous disease. J. Clin. Invest. 33: 1287, 1954.
[22] Ibid.: J. Urol. 72: 1019, 1954.
[23] Ibid.: J. Urol. 76: 213, 1956.

substance of the kidney, appear to be bound to protein in their naturally occurring state (the combination thus formed being termed mucoprotein)[20] Chondroitin sulfate-protein complexes are relatively stable whereas hyaluronic acid-protein complexes dissociate easily[21] It is the chondroitin sulfate mucopolysaccharide which Sylven believed was involved in the calcification mechanism,[2] and it was Sobel who suggested that it was not the chondroitin sulfate mucopolysaccharide alone but a chondroitin sulfate-protein complex which was involved in renal calcification[22] As will be seen later, the investigations of Boyce seem to bear out this impression by Sobel

Previous investigations have indicated that the alteration observed in ground substance, when it becomes calcifiable, is a depolymerization, or a breaking up of the usual multimolecular chain structure into smaller units This presumably opens up reactive groups which can then bind calcium[1]

In any histochemical study the question arises as to what chemical alteration is responsible for a given staining reaction The chemical basis of the von Kossa stain is well known The chemical basis for the PAS stain is known to be a splitting of the 1-2 glycol linkage by the periodic acid with formation of two aldehydes onto which the Schiff's leucofuchsin reagent will then bind[15] However, the application to the vital changes in the kidney is less understood Rubin and Howard[1] state that there is little reason to doubt that the PAS stain when applied to cartilage, stains chondroitin sulfate in the matrix Furthermore, Cobb[23] states that the variation in the degree of staining of a bone is a function of its degree of polymerization—the greater the degree of polymerization, the less the intensity of the staining reaction with the PAS technique

It is uncertain to what extent the above conclusions may be applied to the PAS reaction in the kidney The PAS positive substance in the kidney tubules, especially following the administration of parathormone, is thought to be a mucoprotein[24] Baker proposed that the intense staining reaction to the PAS technique in the areas subsequently or already undergoing calcification, was evidence of the high degree of depolymerization of the mucopolysaccharides of the ground substance of the kidney However, there is some evidence to the contrary in the work of Persson[25] He demonstrated that chondroitin sulfate reacts with PAS apparently independently of its state of polymerization, both if isolated or if mixed with serum He suggested that mucopolysaccharides firmly bound to protein will take a PAS stain and that the intensity of the stain is a reflection of the strength of the mucopolysaccharide-protein bond

There can be little doubt that mucopolysaccharides and mucoproteins are

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[20] Davison, E A and Meyer, K Structural studies on chondroitin sulfuric acid II The glucuronide linkage J Am Clin Soc , 77 4796, 1955

[21] Meyer, K Quoted by Ehrich[19]

[22] Sobel, A E and Burger, M Calcification, investigation of role of chondroitin sulfate *in the calcifying* mechanism Proc Soc Exp Biol Med , **87** 7, 1954

[23] Cobb, Quoted in Engel, M B Mobilization of mucoprotein by parathyroid extract Arch Path , **53** 339, 1952

[24] Engel, M B Excretion of urinary mucoprotein following parathormone in rats Proc Soc Exp Biol Med , **84** 336, 1953

[25] Persson, B H Studies on connective tissue ground substance Acta Soc Med Ups , N S 58, Upsala Almquist & Wiksell, 1953

Mucoprotein polymers in the matrix of bones are broken up by the action of the parathyroid hormone. These mucoproteins, being less able to bind minerals, release calcium into the blood, and then with the dissolution of the bone the mucoproteins themselves are released into the blood where they find their way to the kidney and are excreted through the glomerulus. As they fill the proximal convoluted tubules, these mucoproteins are not yet able to bind minerals. As a result no calcification is ever demonstrated in the homogeneous PAS positive casts. However, as the tubular cells begin to absorb the protein, the droplet-rodlet admixtures form within the cells and the normal process of protein degradation and disposal begins by enzymatic action. This degradation causes the mucoprotein to again become able to bind calcium, and these mucoproteins begin to calcify within the cytoplasm of the tubular cells. As calcification becomes extensive within the cell, the cell walls disintegrate and release myriads of small calcifying mucoprotein granules into the tubule lumens. These granules or droplets have their own built-in enzyme system capable of disrupting this mucoprotein and conceivably of intensifying or furthering the calcifying process. If this explanation be true, it still does not solve the riddle of the origin of the calcium binding mucoprotein which can be found in the urines of patients with calculous disease. According to the explanation proposed, the mucoprotein which finally is expelled in the urine could well contain components of the original mucoprotein filtered through the glomerulus mixed with protein elements from the mitochondria and the other cell constituents, inasmuch as the calcification begins intracellularly.

By means of specialized tissue preparation techniques, it is possible to demonstrate that there is very little similarity between the finer histologic alterations in kidneys undergoing calculus formation due to administration of parathormone and the ingestion of oxamide and uric acid. The assumption that there is a common histochemical denominator for the three types of lithiasis cannot be supported by the histologic findings in these kidneys. If true, the proof would need to come from other approaches.

Although the present study fails to find a histologic similarity between the three types of urolithiasis studied, further study of the diseases produced by ingestion and excretion of uric acid and oxamide may demonstrate a histochemical bridge between them.

The study of the histologic alterations, if any, produced by the addition of toluidine blue and DOCA to the parathormone group is not complete enough to report.

It is felt that the ability to see, stain, and study serially tissues in the finer detail made possible by the method herein described opens a fertile and as yet poorly explored field in the study of renal calcification.

SUMMARY

Preparation of tissues as well as their examination with the phase contrast microscope is described in its application to the study of renal calcification. The method

same process for a number of reasons 1) Both are in droplet form, 2) the intraluminal calcification does not appear to be associated with any changes in the adjacent mucosa, 3) no calcium is seen to deposit in the diffuse PAS positive casts in the tubules, but this will be further explained later The droplet calcification is thought to be clarified by the work of J Oliver[29] who studied proteinurias by means of proteins injected intraperitoneally and intravenously into rats He found that as the protein was excreted through the glomerulus, it began to be absorbed by the proximal convoluted tubules, initially in the middle third of the tubule, and later spreading in both directions As the protein was absorbed, he noted the appearance of droplets within the cells and at the same time noted the disappearance of the rodlets Both rodlets and droplets stain with Janus green, a reaction generally accepted as specific for mitochondria Thus it appeared that these droplets represented more than protein absorbed from the lumen of the tubule, but rather an admixture of protein plus altered mitochondria He further concluded that since mitochondria are rich in enzymes, that it is within these absorbed droplet-rodlet admixtures that protein filtering through the glomerulus is degraded and disposed of

Engel[13] stated that parathormone causes depolymerization and solution of the protein polymers of the bone matrix by means of enzymes This change results in *decreased* mineral binding capacity of the protein matrix and the liberation of calcium and phosphorus He further stated that the mucopolysaccharide complex, observed in the kidney in animals given parathormone in large doses, is derived from blood mucoproteins liberated from the bones Why, then, if the mucopolysaccharide released from the bones by the action of parathormone has a *decreased* ability to bind calcium, should it be expected to attain increased calcium binding power on reaching the kidney? If, as is proposed shortly, the mucoprotein found in the urine of patients with calculous disease, comes through the glomerulus as a protein with decreased mineral binding power, then it must be acted upon for its binding power to be changed This would explain the lack of calcification in the homogeneous PAS positive mucoprotein casts in the tubule lumens

The basement membrane calcification in the parathormone group is not thought to enter into the same process as is represented by the droplet calcification The reasons for this statement are 1) Basement membrane calcification occurred in the animals receiving calcium gluconate alone In none of these animals was there evidence of droplet formation or calcification within the tubular cytoplasm or lumen 2) Basement membrane calcification in the glomerulus (fig 12) is in an area not known to participate in protein absorption It is thought that the basement membrane calcification probably represents a reaction to injury in the kidney in the presence of elevated serum calcium

CONCLUSIONS

It is proposed that the evidence herein presented justifies the following conclusion when viewed in the light of studies by others In calcification associated with administration of parathormone, the sequence of events is as follows

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THE TREATMENT OF PATIENTS WITH URETERAL CALCULI

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The treatment of patients with ureteral calculi has occupied a prominent place in the urological literature for the past 50 years. Forty-six articles have appeared in the JOURNAL OF UROLOGY alone, since it was organized in 1917.

The majority of the stones found in the kidney pass into the ureter and, in many instances, are expelled spontaneously. Of 2,862 patients with calculi admitted to seven hospitals in Richmond, Virginia, during a five-year period, 58.9 per cent had ureteral calculi, and, of 1,732 patients with ureteral calculi reported by six urologists, 12.9 per cent passed stones spontaneously and, of 1,467 patients, 35.9 per cent passed stones following cystoscopic examination (table 1). Of 651 patients admitted to McGuire Veterans Hospital and to the Hospital Division of the Medical College of Virginia, 90 passed stones unaided, while an additional 89 admitted with kidney colic were eliminated from this study because no stone could be found upon admission.

The normal constrictions of the ureter present natural barriers to the passage of stones. The volume, shape and surface of a stone, as well as pathological strictures, or ureteral spasm, may also interfere with spontaneous expulsion.

In the preparation of this paper, we have attempted to correlate reports in the literature concerning management of ureteral calculi and to review our own experience with this problem over the past five years with the hope that we may be better equipped to determine the best treatment for the individual patient with an ureteral stone.

An adequate tabulation of statistical data from the literature is difficult. Some authors who give detailed information regarding the number of stones removed by a given method and the number of cystoscopic procedures required, make no mention of the condition of the kidney or ureter or the location of the stone. Others fail to include the length of time under treatment and make no mention of complications, both of which would be useful to the reader in determining the value of the procedure for his own use. We feel, however, that by grouping the statistical reports of several papers which give similar information, we have obtained a fairly accurate picture of the behavior of ureteral calculi and of the advantages and limitations of different methods of treatment. As an example, in 1925, Bumpus and Scholl reported that of 888 patients with stone in the ureter, 15.3 per cent were in the upper third of the ureter, 7.9 per cent in the middle third, and 72 per cent in the lower third. A group of 2,629 patients, compiled from the statistics of six authors in the more recent literature, showed similar distribution. Sixteen per cent were in the upper third, 14 per cent were in the middle third, and, 70 per cent in the lower third (table 2). Three urologists who reported the segment of the ureter from which stones were removed by cystoscopic manipulation recovered 36 per cent of the stones from the upper third of the

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has been found workable Certain postulations are made concerning the origin of the calcium-binding mucoprotein found in the urines of patients with calculous disease

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with a catheter Marion, in 1910, suggested passing a catheter by a stone and leaving it in place for dilatation and drainage In 1913, Furness described the release of an ureteral calculus by linear fulguration of the ureteral orifice Howard Kelly and Bransford Lewis were also among the early advocates of cystoscopic methods of removing calculi from the ureters]

In 1912, A J Crowell added greatly to the enthusiasm for these procedures when he reported the recovery of 82 ureteral calculi from 95 patients by anesthetization, lubrication and dilatation of the ureter Crowell's enthusiasm for this method of treatment may be understood by his remarks concerning ureterolithotomy He stated that the only unpleasant results since he began the cystoscopic use of anesthesia, lubrication and dilatation occurred in two patients upon whom ureterolithotomy was done A urinary fistula persisted in one of these for several months and the other required nephrectomy because of persistent infection

In 1930, Claude B Squires published a summary of 606 patients treated at Crowell Clinic over a period of fifteen years Stones were recovered in 87 15 per cent of the entire group by cystoscopic procedures Squires stated that the removal of stones by manipulation had been considerably simplified since the procedure was instituted by Crowell At that time, each patient was hospitalized and treated intensively Reactions characterized by chills and fever were not unusual It is apparent that at the time of Squires' report, most of the patients with ureteral calculi were being treated at the Crowell Clinic on an outpatient basis

In 1938, Edwin P Alyea reviewed the literature and discussed the treatment of 236 patients of his own Of this group, 72 per cent of the stones were removed by cystoscopic manipulation and 18 per cent were operated upon Nephrectomy was required in five patients Three died, one following ureterolithotomy, and two were admitted in extremis Alyea's method of treatment consisted of passing multiple catheters, under anesthesia when necessary, twisting and withdrawing them, thereby entangling the stone and removing it If the stone was entangled and difficult to move, elastic traction was applied to the catheters, which usually pulled the catheters and stone from the ureter gradually If the stone could not be dislodged, the catheters were untwisted and removed, one at a time Further effort could be made at a later date or ureterolithotomy done Alyea found that 30 procedures or instruments for removing stones from the ureter had been reported in the literature Since 1938 eleven new instruments or modifications of those already in use have been reported in the JOURNAL OF UROLOGY These consist mostly of modifications of loops and baskets None of these instruments, except probably the looped catheters, have enabled the operator to remove a larger percentage of stones than did Crowell with dilatation of the ureter In recent years, less time has been consumed in recovering the stone but with considerably more risk to the patient [Since 1940, twelve authors have reported 67 instances of ureteral injury Six of these patients required drainage, nephrectomy was necessary in seven and four died At least nine of these injuries resulted from use of the looped catheter Ten of these fourteen reports are either from the

TABLE 1 *Averages from ureteral stones recovered without surgical treatment*

Number Reports	Patients	Spontaneous Passage	Following Examination	By Manipulation
6	1732	223 = 12 9%		
6	1467		527 = 35 9%	
12	4941			3470 = 70 2%

TABLE 2 *Factors influencing transurethral recovery of stones*

1 The location of the stone

Average reports	Patients	Upper Ureter	Mid Ureter	Lower Ureter
3	2629	16%	14%	70%

Removed from each segment of the ureter

6	698	36%	53%	72%

2 The condition of the ureter

	Patients	Spontaneous Passage	By Manipulation
Normal ureter, 1 report	283	8 4%	37 5%
Dilated ureter 1 report	102	3 3%	14%

3 Size of the stone

		Recovered by Transurethral Treatment
Large stones (15 mm or more), 1 report	561	85 9%
Small stones (5 mm or less), 1 report	689	99 7%

ureter, 53 per cent from the middle third, and 72 per cent from the lower third The location of the stone, therefore, becomes of some importance in deciding upon the method of treatment in an individual case

METHOD OF TREATMENT

There are two primary methods of treatment These consist of the passage of catheters or other instruments designed to dilate the ureter and encourage the stone to pass, or, to entangle or grasp it and remove it forcibly from the ureter and ureterolithotomy One gets the impression from the literature that most urologists, or at least those who write, prefer the cystoscopic method of treatment One also gets the impression that, in many instances, this method has been used too frequently

Cystoscopic procedures Since 1889, when Kreissel and his associates reported the recovery of the first ureteral stone, following dilatation of the ureter, the literature has been replete with reports of cystoscopic procedures to rid the ureter of ureteral calculi In 1902, H H Young pried a stone from the ureteral orifice seventy patients at the first attempt with a basket At a second attempt, he could remove only four from the remaining thirty patients

Surgical procedures Like many surgical procedures, the possibilities of ureterolithotomy were discussed many years before it was carried out Valpeau, writing in 1851, mentioned a stone in the ureter demonstrated at autopsy and stated that it might have been removed by a loin incision Thomas A Emmet, in his book "Principles and Practice of Gynecology" published in 1879, described operations for the removal of two stones impacted in the lower end of the ureter, one removed through the bladder and one through a vaginal incision Bardenheuer removed four stones from a ureter by ureterotomy in 1882 Kirkham and Torrey, in 1889 and Twynam, in 1890, are said to have performed ureterolithotomy several times by retroperitoneal operations Morris of London, in 1884, stated that calculi impacted in the intermediate portions of the ureter were practically beyond the reach of the surgeon A similar opinion was expressed by LeDentu, who stated, in 1889, that the portion of the ureter between the entrance and floor of the pelvis must, for the present, be considered as inaccessible to the surgeon A T Cabot, in 1892, concluded that stones in the upper third of the ureter could be removed by the Israel incision, commonly used for operations upon the kidney Cabot agreed with Morris and Le Dentu regarding the inaccessability of the lower third of the ureter and described a procedure similar to the Kraske incision for removing the rectum Cabot also demonstrated the intimate relationship of the ureter to the parietal peritoneum Surgeons who had approached the ureter extraperitoneally near the kidney, gradually found that it could be explored in the same manner lower down In 1910, Gibson described his incision parallel to and above Poupart's ligament, which gave access to the lowermost part of the ureter Three years later Judd contributed to the problem by describing a midline approach to the lower end of the ureter During these early years, very few operations were done for ureteral calculi Jeanbrau, in 1909, could find only 172 cases reported in the literature

It is easy to understand why urologists at that time sought other means of extracting stones from the ureter, furthermore, infection was difficult to control and postoperative drainage often prolonged Urology was gradually evolving as a specialized branch of surgery and, for the most part, was done by general surgeons and gynecologists Many of the earlier urologists confined themselves to diagnostic and instrumental procedures

There is little in the American literature concerning the surgical treatment of ureteral calculi, as compared with discussions of instrumental procedures Of the 41 papers published in the JOURNAL OF UROLOGY, only six were concerned chiefly with ureterolithotomy Of the more recent writers, Lower, Foley, Shaw, and Taylor have made notable contributions to the subject

With improvements in surgical technique and more satisfactory control of infection, stones requiring prolonged dilatation of the ureter with repeated cystoscopic treatment may be removed by ureterolithotomy with less morbidity, and, frequently, with less loss of time The average period of hospitalization for manipulative treatment over the past 30 years is approximately eight days and

West Coast or the Eastern seaboard It is doubtful that urologists in the interior are more skillful or fortunate The average percentage of stones removed by manipulation, reported by twelve men, treating 4,947 patients, was 68 2 per cent If only those were included who are chiefly interested in cystoscopic procedures, the average would be approximately 75 per cent, while, if they were eliminated, the average would be below 60 per cent

A number of factors, other than the classical ones of the size of the stone, hydronephrosis, infection, poor renal function, previous unsuccessful attempts, sex, and congenital anomalies, so frequently quoted from Braasch, should influence the urologist in determining the most desirable treatment for his patient The location of the stone is important The percentage of stones removed from the lower third of the ureter by manipulation is twice that from the upper third It seems, therefore, that in most cases, stones in the upper portion should be given an opportunity to move down, or should be operated upon Dilatation of the ureter definitely reduces the probability of successful transurethral manipulation The force of ureteral peristalsis is reduced, pressure behind the stone is reduced, and, in many cases, inflammatory reaction or fibrosis has occurred around the stone One hundred and two of our patients had dilated ureters The stone was recovered by manipulation in 14 per cent, 49 per cent were operated upon, *and, 3 per cent passed stones unaided One had a nephrostomy and the remainder* were discharged to be followed as outpatients Whereas, of those with normal ureters, stones were removed by manipulation in 37 5 per cent, 16 per cent were operated upon, and 8 per cent passed stones unaided (table 2)

The size of the stone is one of the greatest single factors in determining the method of treatment (table 2) Braasch is quoted as advising against cystoscopic methods when the stone is more than two centimeters in size It is remarkable that stones this size ever pass through the ureter They occasionally do The caliber of the normal ureter averages about six millimeters under normal conditions These large stones are usually composed of phosphates and have grown larger after entering the ureter At times they have grooves in the side, permitting fairly adequate drainage Some writers have mentioned this as an indication of the safety of leaving stones in the ureter for a prolonged period Nephrectomy was necessary, however, *in more than 2 per cent among 1,646 patients reported* by six authors, who mentioned the effect upon the kidney The mortality in this group was 75 per cent Most writers in recent years feel that stones lodged in the upper portion of the ureter, larger than 5 cm , or, in the lower third, larger than a centimeter, should always be removed surgically unless impacted near the ureteral orifice where they can be released by meatotomy We usually remove all ureteral calculi larger than 5 cm surgically, regardless of the location, unless the stone is near the bladder and the ureter easily dilated Other factors, such as an unyielding intramural portion of the ureter, distortion of the base of the bladder, or enlargement of the prostate, may make transurethral methods impractical Efforts to remove stones transurethrally are less apt to be successful if previous attempts have failed One author removed stones from forty of stone was pushed into the renal pelvis and removed by pyelolithotomy in six. Ureterotomy was necessary in one instance to remove the detached tip of a stone basket. One punctured ureter healed spontaneously. There were five deaths. The deaths, with one exception, occurred from uremia. Two of these patients had only one kidney which harbored a stone. One had prostatic obstruction and one, advanced carcinoma of the bladder. One patient with hypertension died of a cerebral accident. The remaining patients were discharged with calculi to be followed in the urologist's office or the outpatient department. The lack of adequate followup records makes it impossible to determine the final disposition of these. They were all patients with small stones and certainly, in most instances, were observed until the stone had passed or they were admitted to another hospital for treatment.

The average period of hospitalization at the Medical College Hospital was 8.4 days and at the McGuire Hospital 10.9 days. Following ureterolithotomy, the patients remained 14.1 days and 15.5 days, respectively. It was interesting to note that those patients who were not subjected to cystoscopic manipulation before the ureterolithotomy recovered three days earlier than those who were. The period of hospitalization was prolonged in many cases because of additional disease, initial assignment to other services, and problems of disposition of indigent patients.

TABLE 5. *Age incidence of ureteral calculi at the Medical College of Virginia, Hospital Division, July 1, 1950 through June 30, 1955*

Age Group	No. of Cases
5–9	1
10–19	9
20–29	42
30–39	86
40–49	114
50–59	78
60–69	36
70–79	16
80–89	1
Total	385

Youngest 6, oldest 85.

TABLE 6. *Sex and race incidence of ureteral calculi at the Medical College of Virginia, Hospital Division, July 1, 1950 through June 30, 1955*

	Total	Male	Female	White	Colored
1950 (July 1–December 31)	45	32	13	39	6
1951	74	41	33	59	15
1952	85	51	34	69	16
1953	82	58	24	61	21
1954	75	59	16	71	4
1955 (January–June 30)	24	21	3	21	3
Totals	385	262	123	320	65

the average postoperative stay for surgical patients about two weeks In recent years, hospitalization has been markedly decreased, especially if the cystoscopic treatment was not tried before ureterolithotomy was done Many patients leave the hospital within a week to ten days following the operation

During a five-year period, we had under observation at the Hospital Division of the Medical College of Virginia and The McGuire Veterans Hospital, 651 patients with a positive diagnosis of ureteral calculi, representing 9 7 per cent of the urological patients admitted to the Hospital Division of the Medical College of Virginia and 5 9 per cent of those admitted to McGuire Veterans Hospital (tables 3 and 4) This discrepancy results from the fact that patients enter McGuire Hospital from a larger area with a relatively small percentage of emergency cases The percentage of Negro patients with stone is the same The age and sex incidence are given in tables 5 and 6 The principal presenting symptoms were pain, hematuria, and fever, in the order named The stone was recovered from 413 patients while in the hospitals, 169 by ureterolithotomy and, in 244 instances, the stone passed spontaneously, or was recovered by cystoscopic manipulation Of the remaining 138 patients, six required nephrectomy The

TABLE 3 *Per cent of urological admissions with the diagnosis of ureteral calculus at the Medical College of Virginia Hospital from July 1, 1950 through June 30, 1955*

Fiscal Year	Total Admissions	White Admissions	Negro Admissions	Calculi White Race	Per Cent White Race	Calculi Negro Race	Per Cent Negro Race	Total Calculi	Total Percentage
'51	702	426	276	68	15 9	14	5 1	82	11 7
'52	849	495	354	64	12 9	15	4 2	79	9 3
'53	805	447	358	65	14 5	19	5 4	84	10 4
'54	767	444	323	66	14 9	12	3 7	78	10 2
'55	915	521	394	57	10 9	5	1 3	62	6 8
Totals	4038	2333	1705	320		65		385	
Averages					13 8		3 9		9 7

TABLE 4 *Per cent of urological admissions with the diagnosis of ureteral calculus at the McGuire Veterans Administration Hospital from January 1, 1950 through December 31, 1955*

Fiscal Year	Total Admissions	White Admissions	Negro Admissions	Calculi White Race	Per Cent White Race	Calculi Negro Race	Per Cent Negro Race	Total Calculi	Total Percentage
'50	651	449	202	31	6 9	5	2 5	36	5 5
'51	689	490	199	35	8 2	7	3 5	42	6 1
'52	796	488	308	43	8 9	8	2 6	51	6 4
'53	710	525	185	37	7 1	4	2 2	41	5 7
'54	639	444	195	34	7 9	6	3 1	40	6 3
'55	717	507	210	50	9 8	6	2 3	56	5 6
Totals	4202	2903	1299	230		36		266	
Averages					8 1		3 6		5 9

infection, or the convenience of the patient Repeated urograms are advisable to determine the progress of the stone and the effect it is having on the kidney until it has passed The interval of these studies varies according to the symptoms presented but should not be more than three months apart An examination is desirable following a severe attack of colic If the expense of repeated intravenous urograms is burdensome, an office cystoscopic observation of the bladder following the administration of indigo carmine will give a good idea of the function of the kidney So long as the stone is making some progress and the kidney has good drainage, active intervention is not mandatory Active treatment is usually necessary when the stone is definitely larger than the narrowest portion of the ureter, if it appears to have a rough or irregular surface, if it is impacted with impairment of the renal function, if there is dilatation of the ureter and/or the renal pelvis, if there is infection and if the stone has been observed six months without evidence of progress A stone in the upper third of the ureter producing any degree of obstruction should be removed by ureterolithotomy If the stone is small and causing no obstruction, time may be allowed, with the hope that it will pass into the lower third of the ureter from which it can be more easily extracted

The majority of stones lodged in the lower third of the ureter can be encouraged to pass by dilating the ureter or by the use of stone baskets or loops The senior author prefers the method described by Alyea In any event, the ureter should be dilated to a size equal to the caliber of the stone before baskets or loops are used A stone impacted in the ureter, one that is accompanied by dilatation of the upper urinary tract or infection, and a stone that is larger than 5 cm in diameter, should, in our opinion, be removed immediately

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CONCLUSIONS

It is apparent that most physicians and patients look upon cystoscopic methods of removing calculi from the ureter as a minor procedure. As a consequence, many ureteral injuries have occurred in recent years and the period of incapacity has been prolonged unnecessarily in many instances. The entire ureter is easily accessible to the skilled surgeon and the disagreeable sequellae of prolonged drainage and persistent infection described by Crowell are rarely encountered.

It is important that an accurate diagnosis be made when possible before deciding upon the type of treatment to be instituted. When the patient is seen during an attack of renal colic, the relief of pain becomes the first consideration. This is usually accomplished by an adequate dose of morphine, accompanied by an antispasmodic drug. Regardless of the fact that physiologists find little evidence of effect on the ureter by these drugs, we have seen additional relief from calcium gluconate too often for it to be coincidental. The senior author is confident that depropanex and octin mucate also have some relaxing effect upon the ureter. Atropine should be given with the opiates. The application of heat, preferably by immersing the patient in a hot tub, is also helpful. Hot water bottles or heating pads are used when the tub is impractical. If pain is relieved, cystoscopic examination or treatment should be deferred and an intravenous urogram made. This will show the condition of the opposite kidney and, usually, the location of the stone and the presence, or absence, of dilatation of the ureter and renal pelvis above the stone. In cases of complete obstruction, contrast material may not appear on the affected side. A nephrogram will indicate recent obstruction. Films taken one or two hours after the injection will often show evidence of function not seen on earlier films. The history and appearance of the stone shadow are helpful in determining the condition of the kidney when no contrast substance appears. A large shadow with a history of previous attack or renal colic is evidence of prolonged back pressure with permanent damage to the kidney.

The patient should be kept ambulatory if practical and after the urogram has been made, should be encouraged to drink large quantities of water. If given a chance, many small stones will pass spontaneously during the 48 hours following an attack. An average of stones passed spontaneously after the patient had seen the urologist, as reported in the literature, was approximately 30 per cent. In our own group of 651 patients, 8 per cent passed the stone spontaneously following hospital admission. An additional 86 patients, admitted during the same period, because of renal colic, were not included in this study because examination failed to disclose any evidence of ureteral stone. Obviously, most of these had passed a small stone.

✓If the preliminary study shows a stone no larger than the caliber of the normal ureter in its narrowest area, 3 mm., and there is good drainage around it, the stone should be given further opportunity to pass unaided, except for the administration of antispasmodic drugs, opiates when needed, and liberal amounts of fluids. These little stones are usually easy to remove and add decidedly to the statistical evidence of the advantages of cystoscopic methods of treatment, but most of them will pass without mechanical aid, if given a chance. In some cases, active intervention is necessary because of uncontrolled pain, accompanying

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URETEROPERITONEAL FISTULA WITH URINARY ASCITES

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In 1930 the author in collaboration with Dr Guy L Hunner[1] reported the case of a patient who, 11 days after subtotal hysterectomy and bilateral salpingo-oophorectomy, had urinary leakage through the cervical stump associated with signs and symptoms of acute right pyelonephritis The acute symptoms quickly subsided, but the leakage of urine continued for 9 weeks when it ceased, and then symptoms and signs of ascites developed At exploration 2 weeks later about 3 liters of urine were evacuated from the peritoneal cavity, and a fistula was found in the right ureter near the stump of the right infundibulopelvic ligament As the ureteral lumen was obliterated below the fistula, the ureter was divided at this level and reimplanted into the fortunately rather voluminous bladder This resulted in complete restoration to normal function and configuration of the right urinary tract Followup observation until 1941 showed a continuation of normal upper urinary tracts bilaterally However, in 1952 the patient returned, and the left kidney was found to be atrophic and functionless as a result of a small calculus obstructing the ureteropelvic junction (fig 1, *A*) Excretory urography, however, showed the right kidney still in good condition (fig 1, *B*)

A thorough review of the literature at the time of reporting this case failed to reveal any similar reported cases However, in 1932, the same authors[2] reported a second case of urinary ascites, in this instance resulting from a spontaneous sloughing and fistula formation in the lower left ureter, occurring 18 months after irradiation for carcinoma of the cervix in a patient in whom a large vesicovaginal fistula developed 6 months after the irradiation An attempt was made to correct the condition by ureterosigmoidostomy, but both ureters were enormously dilated, and the patient was already profoundly uremic from advanced pyelonephritis The patient succumbed to the uremia a few days after operation, and autopsy failed to reveal any remaining carcinoma

The encountering of these two cases early in our professional career stimulated a profound interest in urologic complications resulting from gynecological therapy, both surgical and radiological This interest has led to several contributions dealing with such complications resulting from both types of therapy[3-5]

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The patient had had the tonsils and adenoids removed during childhood, an appendectomy while in high school, and in 1951 a cyst had been resected from the left ovary

The present illness may be said to have begun in 1954 In May of that year she began to experience menorrhagia and metrorrhagia which persisted in spite of conservative treatment until October, when a total abdominal hysterectomy, bilateral salpingectomy, and left oophorectomy were performed Following this operation there was persistent vaginal bleeding for several weeks After discovering that the prothrombin time was only 28 per cent of normal, vitamin K was prescribed, and the bleeding finally ceased During this time Trichomonas vaginitis developed with persistent irritating discharge

From this time until February 1956, the patient remained unwell She never regained normal strength, and suffered from repeated attacks of abdominal pain with chills, fever, and pyuria She stated that these episodes usually followed the partaking of fish, cocktails, or chocolate These attacks were treated with sulfonamides and antibiotics

On February 11, 1956 she was again subjected to surgery, at which time many intestinal adhesions causing partial obstruction were found and released, and the right ovary, which was said to contain both an abscess and endometriosis was removed

Immediately following operation abdominal swelling developed with signs of ascites Probably because of the history of nephritis, the patient was placed upon a salt free diet and given diamox but this treatment was ineffective, and on March 1 paracentesis was done, sufficient fluid being removed to cause a weight reduction of 14 pounds Meanwhile, on February 29 excretory urography had shown rapid excretion of the dye by both kidneys and a right kidney which appeared essentially normal The left kidney showed slight blunting of the calyces (fig 2, A), and films taken 1, 2, and 3 hours after injection of the dye revealed a large accumulation of the radiopaque medium located in the left side of the pelvis and outside of the bladder (fig 2, *B*)

A second excretory urographic examination on April 24 revealed considerable increase in hydroureteronephrosis on the left side and a decrease in the rapidity of secretion and concentration of the dye Delayed films, 2 and 3 hours after injection, showed that the cystic accumulation of the dye in the left side of the pelvis had increased in size but decreased in density of concentration (fig 3, *C*)

Examination on May 28 showed a greatly distended abdomen with unmistakable signs of ascites The patient had intense Trichomonas vaginitis, which subsided completely after one insufflation of aldarsone powder The vagina was shortened, and the vaginal vault was pushed downward by a large cystic mass filling the left side of the pelvis A catheterized specimen of urine was negative microscopically and sterile on culture A diagnosis of left ureteroperitoneal fistula with urinary ascites seemed evident Excretory urography was again done on May 31, and this revealed no visualization of the left urinary tract until 5 hours after injection of the dye, when very faint visualization demonstrated still further increase in the hydroureteronephrosis

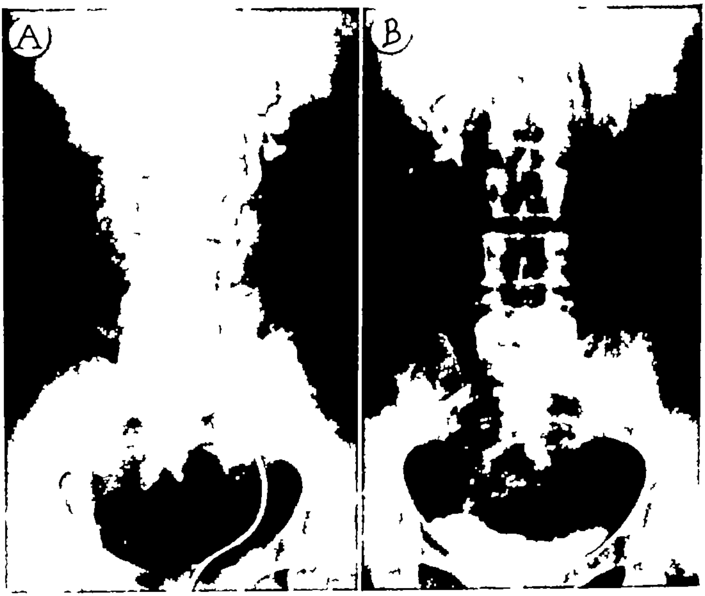

Fig 1 Original case 1 left retrograde pyelogram November 2, 1952 shows atrophied left kidney *B*, excretory urogram November 3, 1952 shows normal right urinary tract and no excretion of dye on left side Small calculus can be seen in region of left ureteropelvic junction

However, until May 28, 1956, we had not seen another case of urinary ascites, and a review of the literature since 1930 has failed to reveal reports of any similar cases, although cases of intraperitoneal accumulation of urine after transection of a ureter, or avulsion of a ureterointestinal anastomosis have occasionally been reported

CASE REPORT

On May 28, 1956 we saw in consultation for Dr A Murray Fisher, Mrs B N, Johns Hopkins Hospital No 739073, aged 35 She complained of abdominal pain and swelling since a gynecological operation performed in her home city, Denver, Colorado, on February 11, 1956 Her general health had been good prior to the course of events which culminated in her present condition She had had scarlet fever rather severely as a child, and acute nephritis in 1944 at which time she suffered from fever and generalized swelling

The menstrual history had been essentially normal until 1954 when the series of events which led to the present condition had begun She had been married for 12 years, and had undergone two normal pregnancies and deliveries resulting in healthy children, nine and seven years of age

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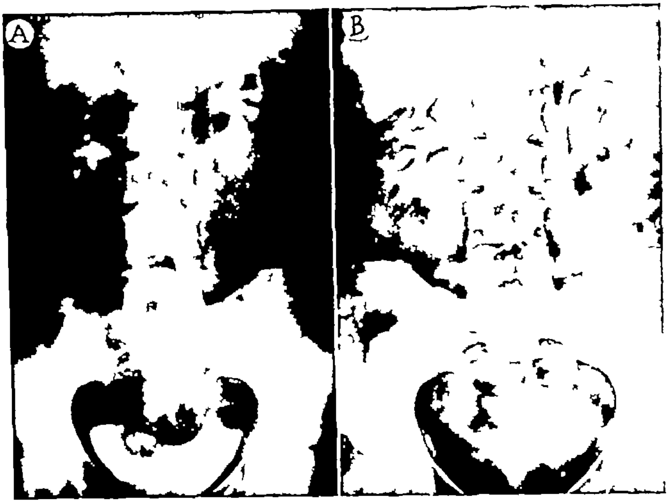

FIG 3 *A*, one-hour exposure on June 18, shows left ureter still moderately dilated throughout *B*, sixteen minute excretory urogram on August 22, 1956, made by Dr Samuel W Downing, of Denver, Colo , shows essentially normal left urinary tract

opening These were passed through the thickness of the bladder wall from within out anterior and posterior to the ureter and securely tied The musculature and serosa of the bladder were brought together over the lower end of the ureter by three interrupted sutures of 000 chromic catgut, and the fundus of the bladder sutured to the upper broad ligament to prevent tension on the anastomosis After releasing a few more adhesions between the sigmoid on the one hand, and the omentum and small bowel on the other, a cigarette drain was placed down to the anastomosis and brought out through the lower end of the incision After closing the abdomen a Foley catheter was inserted into the bladder, and the polyethylene tube was securely strapped to this catheter

The patient withstood the operation well, and the convalescence for the first 5 days was remarkably uneventful Two-hour intravenous phenosulfonphthalein test on the third postoperative day yielded 70 per cent through the Foley catheter and 20 per cent through the tube from the left kidney

On June 6 the patient suffered chills, fever, and pain in the left renal area The urine from both tube and catheter contained pus, and on culture yielded mixed organisms Paracolon, coli-aerogenes group Beta enterococci, and Streptococcus faecalis This mixture of organisms showed a variety of sensitivities, but furadantin and neomycin seemed to be the drugs most strongly indicated Accordingly, furadantin was administered by mouth, and the polyethylene tube was irrigated several times daily with neomycin Under this treatment, the febrile episode subsided by June 10, after which convalescence continued favorably

The catheter and tube were removed on June 14, two weeks after operation, and on June 18, excretory urography showed fairly good visualization of the left kidney in 10 minutes, and complete visualization and considerable reduction of the hydronephrosis in 20 minutes The ureter, however, was not filled until an

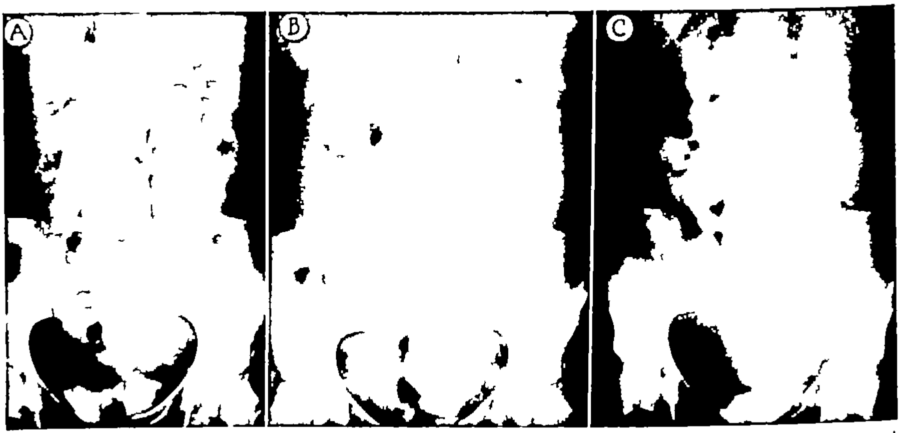

FIG 2 *A*, twenty minute excretory urogram February 29, 1956, 18 days after operation during which left ureter was injured Left kidney is functioning well, but pelvis and calyces are slightly dilated Extreme lower end of left ureter is not visualized and just above this the ureter appears dilated and distorted Small accumulation of opaque medium may be seen in left side of pelvis outside ureter and bladder *B*, two-hour intravenous urogram also on February 29 shows great increase in accumulation of dye in left side of pelvis, and delay in emptying of left urinary tract *C*, two-hour film on April 24 shows great increase in size and decrease in density of accumulation of opaque medium in left side of pelvis as compared with *A*

Considerable thought was given as to whether to perform a left nephrectomy, or to attempt to correct the damage to the left ureter The conservative procedure was chosen and carried out on June 1 After opening the abdomen a large quantity of urine was evacuated from the general peritoneal cavity The sigmoid colon was bound to the inferior pelvic wall by a sheet of edematous adhesions approximately 5 mm or more thick Behind the sigmoid colon and these adhesions was the large cystic accumulation of fluid which had been demonstrated in the earlier x-rays Most of the loops of small bowel were agglutinated by adhesions The thick adhesions binding the colon to the pelvic wall were dissected free and the cystic fluid evacuated Inspection of the left pelvis then revealed a plaque of grumous yellow urinary sediment over the mid broad ligament portion of the left ureter Removal of this revealed an opening into the ureter into which a probe could be easily inserted and passed upward, but it could not be passed downward The ureter, therefore, was dissected free for about 5 cm above the perforation and divided at the point of perforation Short lateral slits were made in each side to form a fish mouth opening, after which a polyethylene tube with an outside diameter about equal to that of a 10F ureteral catheter was inserted upward to the renal pelvis An incision approximately 3 cm long was then made through the muscular coats of the bladder at the most accessible location for inserting the ureter, and the bladder mucosa was perforated only at the lower end of the incision The free end of the polyethylene tube was inserted into the lumen of a male catheter introduced into the bladder during preoperative preparation The tube and catheter were sutured together and drawn out through the urethra The free end of the ureter was drawn into the bladder by transfixion sutures of 000 chromic catgut which had been placed in each lip of the fish mouth of urinary tract infections due to Escherichia coli by means of both of these drugs These results would seem to indicate that organisms may migrate by some means from the bowel into the urinary tract, and that the use of such drugs halts the infection at its source The condition of the bowel found at operation in the case here reported would certainly seem to have been such as to favor such bacterial migration

SUMMARY AND CONCLUSIONS

A third case of urinary ascites due to ureteroperitoneal fistula is added to the two cases reported years ago The first and third of these cases illustrate strikingly the wisdom of reconstructive procedures designed to save the kidney whenever possible, even though at the time the function of the kidney may appear to be greatly impaired

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hour after injection of the dye, and then showed moderate dilatation throughout (fig 3, *A*) At cystoscopy on the same day, the artificial left ureteral orifice was easily located and appeared healthy

On June 19 the patient experienced a second but milder febrile episode with chills This followed an enema, and the patient seemed convinced that most of her febrile episodes had followed enemas For this reason furadantin and neomycin were prescribed, orally, and she became afebrile by June 22 Urine obtained on June 26 was negative microscopically, but on culture yielded Alcaligenes faecalis which was resistant to all drugs for which its sensitivity was tested No further complications developed, and the patient was discharged and returned to her home on July 3

At home she has been followed by Dr Samuel W Downing who had excretory urography repeated on August 22 This examination showed a normal left urinary tract, both anatomically and functionally (fig 3, *B*) In September the patient experienced a brief episode of cystitis which responded to triple sulfonamides, and aside from that has remained well

DISCUSSION

It seems almost incredible that three cases of urinary ascites from ureteroperitoneal fistula should have come under our observation, and that no similar cases should be found in the literature This leads us to suspect that similar cases either have not been correctly diagnosed, or else not reported We do not believe that we should be entitled to a monopoly of this condition However, the condition probably does occur with great rarity The operation during which most ureteral injuries occur is hysterectomy, and since in recent years most hysterectomies have been of the total variety, if a ureter is injured, a ureterovaginal rather than a ureteroperitoneal fistula will form

The results in the original case reported in 1930, and in the one reported here indicate the wisdom of attempting to conserve the kidney in cases of ureteral injury, even though its function seems greatly impaired The length of time during which a kidney can withstand partial or complete obstruction and still regain essentially normal function is not definitely known In the case reported in 1930, eighty-eight days had elapsed between the operation in which the ureter was injured and that in which it was repaired In the present case, the interval was 110 days In a recent report of urinary tract injuries in general,[7] one case was recorded in which a kidney recovered essentially normal function after 18 days of complete obstruction by a ligature

The apparent effective control of renal infection by neomycin administered orally offers an interesting speculation This drug is said not to be absorbed into the system from the digestive tract, or if so, to only a very slight degree However, the same is true of sulfasuxidine (succinylsulfathiazole) and sulfathalidine (phthalylsulfathiazole) Some years ago[9, 10] we published results of successful treatment

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marked residual urine Microscopically the urine was almost always reported negative, but did contain some albumin, and the urine cultures were almost always positive All had been admitted to the hospital on several occasions or were considered pediatric diagnostic problems and urologic consultation had been sought as an end resort when everything else had failed We have attempted to summarize our experiences with this second group of cases to determine if there are any routine objective means of recognition

SYMPTOMS

The subjective symptoms were of little or no value The mother sometimes noted evidence of straining to urinate, the baby would cry or become red in the face, or would wet more diapers than normal These however, were not constantly noted The predominant symptoms were confined to the gastrointestinal tract These children were all considered feeding problems had nausea and diarrhea and failed to develop and gain weight

CLINICAL COURSE

The clinical course was remarkably similar in almost every case After delivery the child would be readmitted in a state of malnourishment, dehydration, and acidosis The patients, almost inevitably, would be considered feeding problems but despite all measures and complete investigation of the gastrointestinal tract would continue to do poorly and fail to gain weight

LABORATORY FINDINGS

The blood urea nitrogen or nonprotein nitrogen was elevated, even though there was no residual urine The CO_2 combining power was decreased, indicating definite acidosis It was our impression that the lowered CO_2 and elevation of serum nitrogen suggested bladder neck obstruction of low degree with resultant pressure on the kidneys leading to renal acidosis The urine, as already mentioned, was negative on microscopic examination, contained small amounts of albumin, and showed infection on culture The intravenous pyelograms were universally poor in quality, but normal anatomically One must avoid the mistake that is so common in dealing with pediatric patients of assuming that the infant is a small adult and exhibits the same responses as adults Campbell has long ago pointed out the fallacy of such reasoning [5]

However, in considering the elevated nonprotein nitrogen or blood urea nitrogen and the lowered CO_2 combining power as definite diagnostic indications of bladder neck obstruction, one should remember that the renal function of the newborn is vastly different from that of the adult In fact, it is so vastly different that if one is not familiar with the renal function of the newborn, the objective elevation of the serum nitrogen and decreased CO_2 combining power can also be a diagnostic pitfall

Since we have found this to be so important, we would like to digress a moment and consider briefly the recent developments in the field of functional physiology

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RENAL ACIDOSIS AND UREMIA IN THE NEWBORN DUE TO UNRECOGNIZED BLADDER NECK OBSTRUCTION

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In children, the most commonly reported symptoms of bladder neck obstruction are those which are usually associated with infection. Urologists have become increasingly aware that many urinary infections in children, particularly chronic or intermittent infections, are due to bladder neck obstruction.[1-4] The lack of subjective symptoms in infancy is probably responsible for the scarcity of reports upon the clinical recognition of bladder neck obstructions in the very young. Burns and associates have already pointed out the over-emphasis which has been placed on congenital urethral valves as the cause of bladder neck obstruction in children and report that the vast majority of cases of bladder neck obstructions which they encountered were due to bladder neck contractures. We have also found this to be true; while congenital valves are occasionally seen, contractures of the bladder neck are far more common.

We became interested in the early recognition of possible bladder neck obstruction in infants a number of years ago when a 14-week-old male infant, malnourished and underweight, was readmitted to the hospital because of diarrhea and vomiting. No cause for the difficulty had been found in the gastrointestinal workup. The urine had been reported negative on microscopic examination, but a culture showed organisms. The nonprotein nitrogen was elevated and the CO_2 combining power lowered. Intravenous pyelograms were poor, but showed no anatomical deformity. Observation cystoscopy showed a minimal contracture of the bladder neck, but the infant made a dramatic improvement following a transurethral resection of the bladder neck.

We believe it is a well accepted fact that minimal degrees of bladder neck contracture are difficult to diagnose in the newborn by observation cystoscopy alone, and might very well represent merely a subjective opinion. In attempting, therefore, to evaluate the diagnostic measures of value in such cases we found that the patients could be divided into two well defined groups. One group showed similar findings to those in adults with bladder neck obstruction, namely, residual urine, dilated bladders, ureteral reflux, and hydronephrosis in varying degrees up to frank bilateral megaloureters. Such cases, even in infants, present little or no diagnostic difficulties. In almost all cases the urine was infected, and routine diagnostic urological measures commonly revealed the source of the difficulty and led to prompt correction of the obstruction.

In the second group, however, there were almost no x-ray changes and no

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Read at annual meeting of American Urological Association, Pittsburgh, Pa., May 6-9, 1957.

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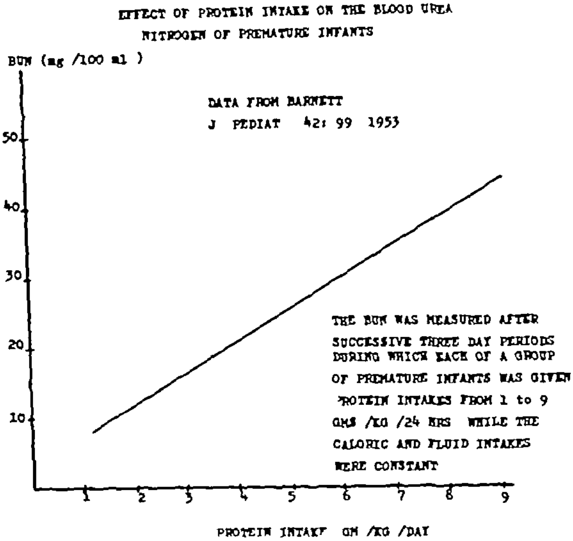

FIG 1

In all cases the values rose to abnormal levels with increased protein intake Their results are illustrated graphically in figure 1 Further experiments showed that this rise was due to increased production of urea rather than a decrease in urea clearance A single elevation of blood urea nitrogen, therefore, must not be used clinically to evaluate renal function in infants, particularly unless the nitrogen intake is known The acid base regulation of the body by the kidneys has been investigated in young infants only to a limited extent[13] [15] If given oral ammonium chloride, young infants excrete less ammonia and lose more sodium This would explain the development of acidosis in young infants fed protein milk formulas In table 1 a comparison of the renal function between adults and children is made

It is common but erroneous practice to associate the intravenous urogram with renal function The clinical experiences with the newer high concentration intravenous media show an increased percentage of satisfactory urograms[16] The mechanism of urokon excretion has been studied by Porporis, Elliott, Fischer, and Mueller[17] Since there is little difference in chemical structure and percentage of dye, the same findings should apply to miokon and hypaque, and should apply also to infants as well as adults These investigators found that the inulin clearance is unaffected by the intravenous injection of urokon and that the clearance of urokon is similar to inulin at plasma concentrations of urokon usually reached by the intravenous injection of amounts commonly used in intravenous urography This is of great clinical importance since only those patients with shock, of the kidney of infants and children The important separate functions of the adult kidney that can be measured are the effective renal plasma flow, rate of glomerular filtration of water, and rates of absorption and excretion by the tubules of various endogenous and exogenous substances[6] The problems of doing such studies in the average hospital on infants or children make them unsuitable for general clinical application[7] It is very important, however, for those of us who see pediatric patients to be aware of the differences that have been shown to exist in the renal function, particularly in young infants The literature, quite understandably, is voluminous, and we have tried to include only the most applicable clinical work Marples and Lippard in 1932[8] suggested that the high chloride serum levels of newborn infants were due to the decreased ability to excrete chloride Barnett[9], using inulin clearance studies, showed that the values in infants ranged from 25 to 50 per cent of adult figures when corrected for surface area, indicating that kidney function is not fully developed in early life The rate of maturation of renal function measured by glomerular filtration has been reported by West, who says that some infants may reach adult values corrected for surface area as early as 10 to 20 weeks[10] Rubin's figures, however, show that in infants under 6 months of age, none of the values were within adult range[11]

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[13] Gordon, H H, McNamara, H and Benjamin, H R Pediatrics 2 290, 1948

[14] Hoffman, W S, Parmelee, A H and Grossman, A Am J Dis Child, 75 637, 1948

[15] Darrow, D C, da Silva, M M and Stevenson, S S J Pediat, 27 43, 1945

[16] Barry, C N and Rose, D K J Urol, 69 849, 1953

[17] Porporis, A A Elliott G V, Fischer, G L and Mueller C B Am J Roentgenol, 72 995, 1954

Although we seldom think of it as such, the most commonly used clinical renal function test is the measurement of the blood urea nitrogen or of the nonprotein nitrogen which we interpret as providing estimates of the urea clearance and hence paralleling changes in the glomerular filtration rate In so doing we assume that the rate of excretion of urea by the kidney is constant and that the urea clearance maintains a constant relationship to the inulin clearance In the case of nonprotein nitrogen, we also assume that blood urea nitrogen represents a constant proportion of nonprotein nitrogen The rate of urea excretion by the kidney, and therefore blood urea nitrogen, is markedly influenced by the protein content of the diet The ratio of urea clearance to inulin clearance and the ratio of blood urea nitrogen to nonprotein nitrogen are not constant Thus blood urea nitrogen is a better test than nonprotein nitrogen Either, however, gives only a rough approximation of the glomerular filtration rate The factors chiefly influencing blood urea nitrogen are 1) protein intake and retention, and 2) variations in rate of urine flow which alter the urea clearance in the absence of significant changes in glomerular filtration rate[12]

Goldstein, Barnett and McNamara[12] have measured blood urea nitrogen after successive three-day periods during which each of a group of premature infants was given formulas providing protein intakes ranging from one to nine grams per kilogram per 24 hours, while the caloric and fluid intakes were held constant

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[6] Smith, H W The Kidney Structure and Function in Health and Disease New York Oxford University Press, 1951

[7] Barnett, H L and Sereni, F Pediat Cl North Amer **2** 191 1955

[8] Marples, E and Lippard, V W Am J Dis Child, **44** 31, 1932

[9] Barnett, H L Pediatrics, **5** 171, 1950

[10] West, J R Smith, H W and Chasis, H J Pediat, **32** 10 1948

[11] Rubin, M I, Bruck, E and Rapoport, M J Clin Investig **28** 1144, 1949

[12] Barnett, H L and Vesterdal, J J Pediat, **42** 3, 1953

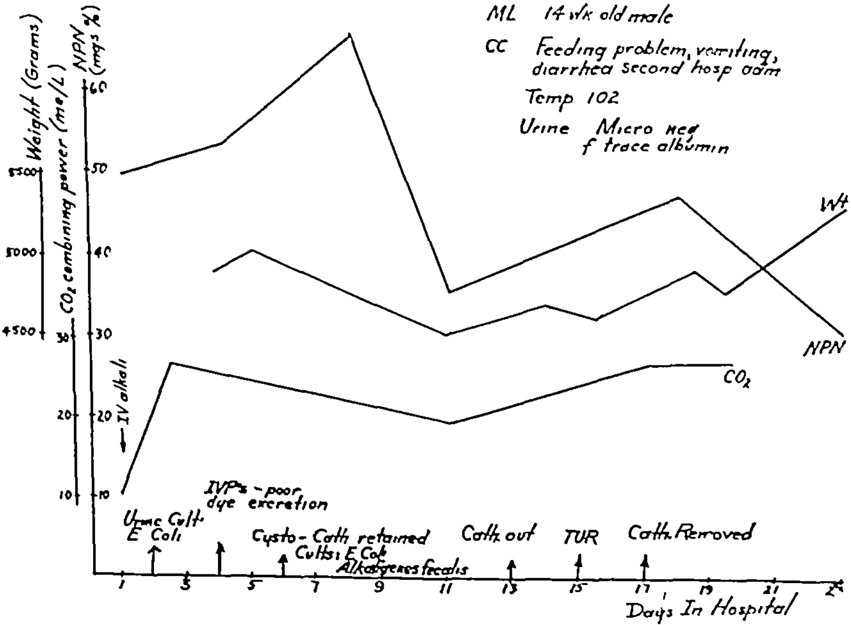

FIG 2

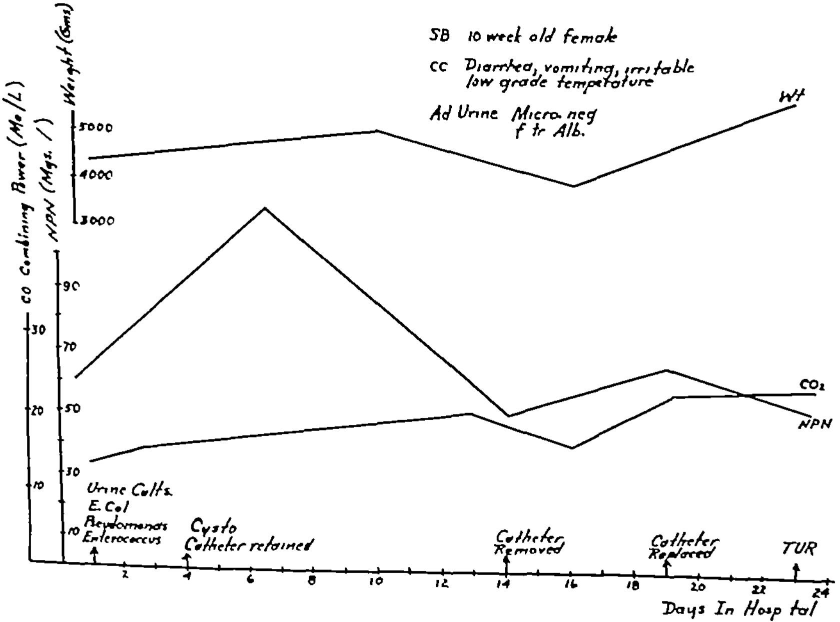

FIG 3

caloric intake and fluid intake the same and determining the effect of urethral catheter drainage on either blood urea nitrogen or nonprotein nitrogen and CO combining power If the blood urea nitrogen or nonprotein nitrogen falls, we believe that this is further confirmatory evidence that a bladder neck obstruction

TABLE 1 *Known functional differences between the adult and infant kidney*

	Men	Women	Children	Infants
Glomerular filtration rate (G F R) C_{IN} (inulin clearance) ml /min per 1 73 sq M	127	118	123	30–50% of adult values
Standard deviations		15–20		
Effective renal plasma flow (ERPF) C_{PAH} or C_D (diodrast or PAH clearance) ml /min per 1 73 sq M	655	600	634	20–40% of adult values
Standard deviations	100–150			
It has not been proven that PAH and diodrast are removed from the plasma in one passage through the kidney as it has in the adult but it is assumed to be so				
Filtration fraction (C_{IN} C_{PAH}	0 2			0 3–0 4
Standard deviations		0 2–0 4		
Maximum rate of tubular excretion and reabsorption (T_M) mgs /min per 1 73 sq M	77			15–40% of adult values
Standard deviations	10–15			

Figures from Barnett H L , J Ped **42** 99 1953

vascular occlusion, advanced renal disease, or ureteral obstruction will show any deviation in the time or amount of dye excreted It further indicates that a satisfactory intravenous urogram is not always indicative of a normally functioning kidney In the infant, it is even more difficult to make any estimate of renal function based upon intravenous urograms, because of the many technical factors involved If one predicates moderate ureteral obstruction due to the bladder neck obstruction, however, it would be expected that these infants would show poor intravenous urograms, and this has been found to be true in our cases

We feel, then, that in the group of infants presented as representative of the problem, it is obvious that there is very little renal reserve present If definite urinary obstruction at the bladder neck is present, causing nitrogen retention and acidosis, the most conservative measure would be corrective surgery of the bladder neck On the other hand, surgery should definitely not be advised unless absolutely necessary

It is a comparatively simple procedure to rule out those cases of elevated non-protein nitrogen or blood urea nitrogen with a lowered CO_2 combining power due to high protein feedings or protein milk formulas As a further clinical test, however, retention urethral catheter drainage was instituted, keeping the diet, is present If one is still suspicious of the diagnosis the retention catheter can be removed to determine the effect on the blood urea nitrogen Two cases in which this was done are illustrated in figures 2 and 3 It can be seen that when the urethral catheter was removed after the nonprotein nitrogen had reached normal levels it immediately became elevated falling to normal levels again after the catheter was replaced

The bladder neck obstruction may be corrected either by transurethral resection of the bladder neck or retropubically The method that one selects is probably based upon his ability with that particular route of surgery however it is our opinion that in this age group of patients transurethral resection is very definitely the procedure of choice The functional results are as good the procedure is better tolerated by the patient and the operative risk is definitely less than with a retropubic approach

It has been stated by proponents of the retropubic route that subsequent contractures of the bladder neck are more common after transurethral resection With this we cannot agree since if the transurethral resection is adequately accomplished and all fibrotic tissue around the bladder neck removed down to the normal muscle fibers there is no tendency to late contraction of the bladder neck Needless to say urethral stricture following transurethral resection is due to errors in technique namely trauma to the urethra in passing the infant resectoscope The infant's urethra should be accurately and carefully dilated before the resectoscope is passed and either the 14 or 16F infant Stern-McCarthy instrument used In support of our contention we have selected four representative cases in which this was done three have been followed for at least four years and none has shown any evidence of late contracture All have remained well and all have developed into perfectly normal children The cases are illustrated in figures 2 to 5

SUMMARY

In young infants renal function is poorly developed as compared with the adult and less renal reserve is present

Minor degrees of bladder neck obstruction in the young infant can lead to unexplained uremia and acidosis

In the young infant the symptoms have been largely gastrointestinal and many have been considered as feeding problems in the past

It is possible to diagnose accurately the bladder neck contracture by objective findings and not to depend upon subjective findings although these of course are important

Care must be taken to rule out elevation of the blood urea nitrogen and lowering of the CO_2 combining power due to high protein or protein milk diets

Adequate transurethral resection of the bladder neck has been curative and the late postoperative results have been good

3720 Washington Ave St Louis 3 Mo

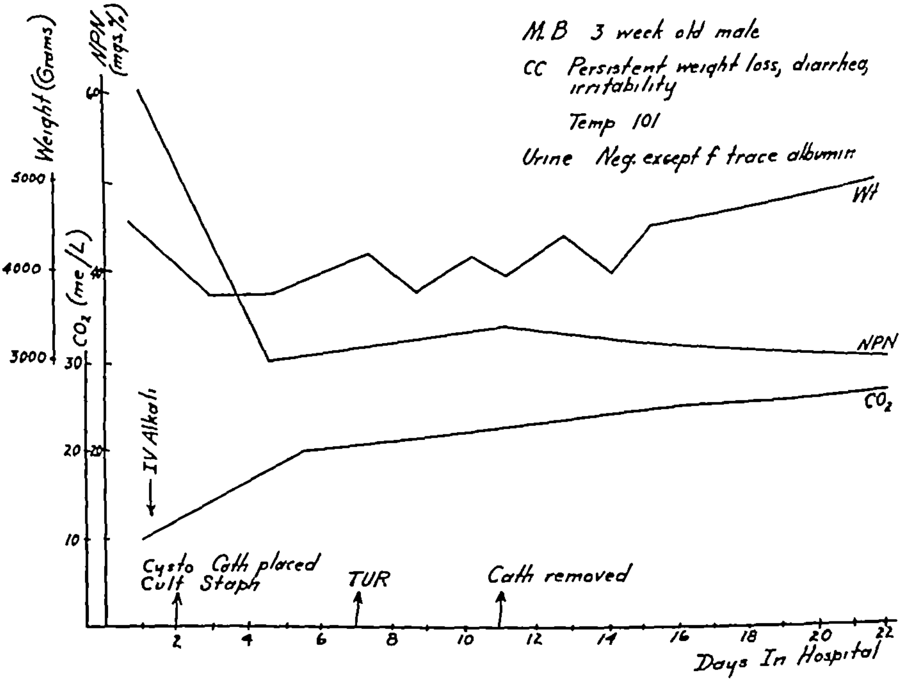
M.B 3 week old male
CC Persistent weight loss, diarrhea, irritability
Temp 101
Urine Neg. except f trace albumin
Weight (Grams)
NPN (mgs%)
CO2 (me/L)
5000
4000
3000
30
20
10
60
40
30
20
IV Alkali
Wt
NPN
CO2
Cysto Cult Staph
Cath placed
TUR
Cath removed
2
4
6
8
10
12
14
16
18
20
22
Days In Hospital

FIG 4

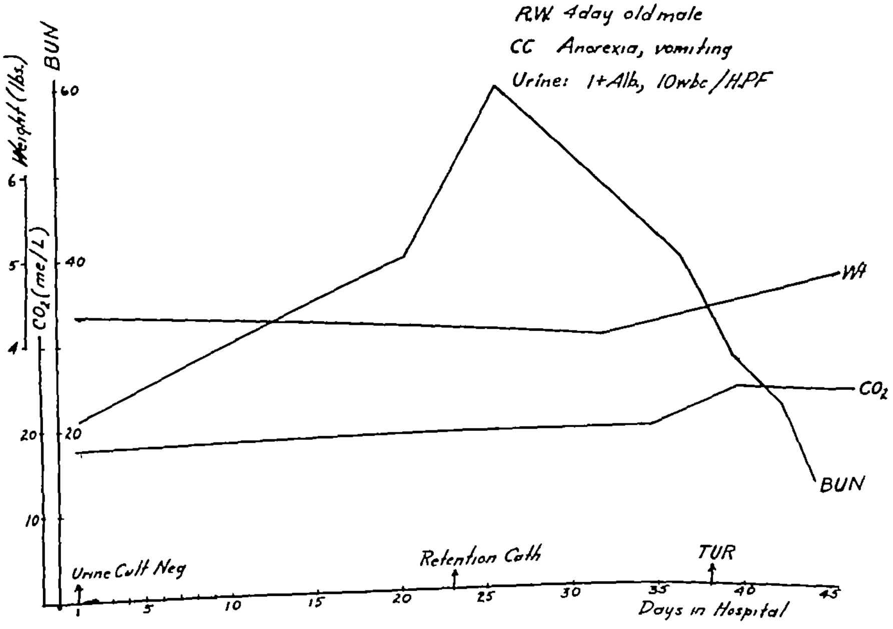
R.W. 4 day old male
CC Anorexia, vomiting
Urine: 1+Alb, 10 wbc/HPF
Weight (lbs.)
BUN
CO2 (me/L)
6
5
4
20
10
60
40
20
Wt
CO2
BUN
Urine Cult Neg
Retention Cath
TUR
1
5
10
15
20
25
30
35
40
45
Days in Hospital

FIG 5

Our series consists of six patients, all grade 3, according to Hand, who were studied and operated upon between December 1955 and February 1957 All were women The range in age was from 35 to 69 with an average age of 54 Their symptoms had been present between five and twelve years, with an average of 9 2 years All had severe pain All had had the large variety of treatment prescribed, but only one had had a partial cystectomy Two had gross hematuria In every instance, the ulcers had been observed cystoscopically on several occasions

Indications for this procedure consist of cases with grade 3 lesions, in which all known methods of treatment have failed, save cystectomy, in which nerve blocks produce a definite increase in bladder capacity

METHOD

Preoperative observations Prior to operation, selective blocks of the sacral nerves were made under radiographic control Bladder capacity was determined before and after block, and the intravesical pressure at maximum distention was also established The results are recorded in table 1 Operation was not advised in those cases where there was little increase in capacity following block, in accordance with Meirowsky's work

Operative exposure A midline incision was made over the sacrum The musculature was stripped back beyond the sacral crests bilaterally The sacral foramina were identified by reference to the spinous process of the fifth lumbar vertebra

TABLE 1 *Observations at the time of block*

Patient	Nerves Blocked	Bladder Capacity Cubic Centimeter		Bladder Pressure mm H20	
		Before	After	Before	After
1 B H	S 3	45	170	Not measured	
2 H I	S 3	30	200	600	430
3 M P	S 3	175	200	320	240
4 C A	S 3	290	380	170	160
5 R S	S 3	25	60	240	220
6 A H	S 3	85	175	220	250

TABLE 2 *Observations at operation*

Patient	Nerves Stimulated Bilaterally	Change in Bladder Pressure mm H20	Rectal Sphincter Spasm	Levator Ani Contraction	Nerves Divided Bilaterally
2 H I	S 2	320–450	Marked		
	S-3	320–380	Slight		S 3
4 C A	S 2	None	Marked	None	
	S-3	200–600	None	Moderate	S 3
5 R S	S 2	None	None	Moderate	
	S-3	240–600+	Marked	None	S 3
6 A H	S 2	380–440	Slight	Slight	
	S-3	380–600	Slight	Marked	S 3

No stimulation cases 1—3

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SELECTIVE SACRAL NEURECTOMY IN INTERSTITIAL CYSTITIS

WILLIAM A. MILNER and WILLIAM B. GARLICK

Ever since Hunner first introduced and named a distressing condition of the bladder, which he called interstitial cystitis or elusive ulcer, the urological world has been plagued with this condition. The very nature of the disease, with its great variability, and at times tenacity, has made it a very difficult and confusing entity to diagnose and to treat. All one has to do is to review the literature and find the multiplicity of treatment to realize that this is not a simple problem.

It is not the desire of the authors to reiterate or review the voluminous literature, but merely to call attention to a palliative procedure designed for the intractable cases where all types of treatment have failed. It is with these cases, which fit into the grade 3 classification of Hand, and followed by Engel, Meads and O'Conor, that we are concerned. As Hand states, "Grade 3 represents the most advanced stage of the disease. In the greatest number of cases the lesions were recorded as being "diffuse." The mucosal surface was pale and often showed linear scars of old lesions. While there was bleeding on distention, the dominant finding was a zigzag fissuring which suggested a split along the lines of the underlying vascular network and muscle bundles. Bladder capacity was greatly diminished, being 150 cc or less." All of our cases qualify for grade 3. Each one has been treated with many types of therapy including clorpactin as described and advocated by O'Conor. Occasional relief was obtained but in most instances was temporary. Therefore, a new approach to the problem was sought.

A. M. Meirowsky by personal communication to our late professor of neurosurgery, Dr. Eldridge Campbell, informed him of two cases of Hunner's ulcer treated by differential sacral neurotomy. Dr. M. K. Moulder of the Department of Urology suggested this and combined with Dr. Meirowsky of the Department of Neurosurgery, Vanderbilt University School of Medicine, to pioneer in this procedure on selected cases. This preliminary work was published in the JOURNAL OF UROLOGY in 1956. Great emphasis was laid on the selection of the patient, for it was felt that if the patient could not be relieved of the two most distressing features, namely, intractable pain and frequency, then the procedure would not be worthwhile. Meirowsky discovered earlier, in his extensive work with paraplegics, that differential sacral neurotomy increased bladder capacity due to a reduction in the parasympathetic outflow to the detrusor and of the sacral somatic outflow. From this work came the idea to try this procedure in Hunner's ulcer.

The Department of Neurosurgery, headed by Dr. Eldridge Campbell until his untimely death, then by Dr. Robert Whitfield, became absorbed in this problem. Our department was more than interested in liberating a few miserable souls whose whole existence centered around the bathroom. We supplied the ammunition and the neurosurgeons fired the gun.

Read at annual meeting of American Urological Association, Pittsburgh, Pa., May 6-9, 1957.

TABLE 5 *Followup reports*

Patient	Time Post-op	Bladder Capacity Cubic Centimeters	Frequency	Healing of Ulcer	Symptoms
1 B H	17 mos	450	4 hr	Yes	None
3 H I	14 mos	375	3 hr	Yes	None
2 C A	12 mos	300	3½ hr	Yes	None
4 M P	11 mos	150	2 hr	No	Pain and bleeding
5 R S	13 mos	160	3 hr	Yes	None
6 A H	6 mos	430	4 hr	Yes	None

hypalgesia and perineal numbness were present The hypalgesia was not too severe and disappeared after a few weeks Not one patient complained of hypalgesia, which was of minor importance when compared to the previous vesical difficulties None of the patients had residual urine or any difficulty in voiding

Table 5 represents a followup of these cases at the present time The first, case 1, 17 months since operation, is the oldest patient in this group and has obtained the best result Her bladder shows no cracking, holds 450 cc with no residual, and she is comfortable She drove to our office for followup examination and rode 3½ hours in the car with no difficulty Her first trip, preoperatively, was a nightmare of stopping every 15 minutes with marked pain As you can see, the other results are gratifying In only one patient has cracking and ulceration persisted and even though her frequency is relieved, she still has some pain and bleeding She is the only patient who underwent partial cystectomy prior to surgery Repeated biopsies fail to reveal malignancy

This is a small series with a short followup, but the results warrant a continuance of this procedure in selected cases As more and more are done, our knowledge will increase and the evaluation of this treatment can then be estimated It may be necessary in some cases to section S-2, as has been performed in certain cases of neurogenic bladder

We are indebted to Drs Moulder and Meirowsky for initiating this procedure, and to Drs Campbell and Whitfield for so ably carrying on this work

SUMMARY

Observations upon six patients suffering from severe interstitial cystitis, in whom other methods of treatment failed, are recorded

In all cases, the third sacral nerve contributed to bladder detrusor activity

In two cases, the second sacral nerve contributed to bladder detrusor activity and in two cases no response

In five cases, bilateral section of the third sacral nerves produced subjective relief of symptoms and objective evidence of improvement with healing of the bladders One case, with previous partial cystectomy, has subjective relief of symptoms, but the bladder has not completely healed

75 Willett St, Albany N Y

The second and third sacral foramina were unroofed, the nerves (anterior primary rami) freed, and in the four later cases, the second and third sacral nerves stimulated in turn, while cystometrographic observations were made A member of the group estimated by digital examination the contractions of the anal sphincter and of the levatores ani This stimulation of the nerves at the time of operation was an innovation conceived by Dr Campbell after the first two cases had been done, for he felt that this would aid in selecting the proper nerves to be sectioned The third sacral nerves were sectioned and a small piece removed to prevent regeneration, in all six cases Hence the term, neurectomy rather than neurotomy

Observations at operation Table 2 records the results of stimulation of S_2 and S_3 in the last four cases In two instances S-2 gave marked bladder response, but in the other two only S-3 had any effect on the bladder S-2 seemed to have more effect on the rectal sphincter and levator ani contraction, but no conclusions can be drawn from this small experimental group

RESULTS

Table 3 records the postoperative results, as far as the bladder is concerned, in the first few weeks following surgery Frequency and pain were relieved in all patients except one and she was improved as far as frequency was concerned, but still had some pain and an unhealed ulceration All the other bladders showed good capacity and no evidence of ulceration

Table 4 shows the postoperative neurological deficits In spite of some diminution in rectal sphincter tone, no rectal incontinence developed As you can see,

TABLE 3 *Postoperative results (bladder)*

Patient	Nerves Divided	Bladder Capacity Cubic Centimeters		Frequency		Healing of Ulcer
		Pre-op	Post-op	Pre-op	Post-op	
1 B H	S 3	45	180	10 min	4 Hr	Yes
2 H I	S 3	30	300	20 min	3 Hr	Yes
3 M P	S 3	175	200	15 min	3 Hr	No
4 C A	S-3	290	300	1 hr	6 Hr	Yes
5 R S	S 3	25	75	10 min	2½ Hr	Yes
6 A H	S 3	85	195	30 min	4 Hr	Yes

TABLE 4 *Postoperative deficits*

Patient	Rectal Sphincter Tone—% of Normal	Rectal Incontinence	Neurologic Deficit
1 B H	75%	None	None
2 H I	75%	None	Hypalgesia lateral, left thigh
3 M P	75%	None	Hypalgesia S 3 absent gluteal reflexes
4 C A	50%	None	Perineal numbness subjective
5 R S	75%	None	Absent ankle jerks
6 A H	75%	None	None

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ILEOCYSTOSTOMY FOR NEUROGENIC BLADDER

JUSTIN J CORDONNIER

From the Division of Urology, Department of Surgery Washington University School of Medicine St Louis Mo

With improvements in surgical management and chemotherapy the problem of management of the urinary bladder in cases with various types of paraplegia has assumed increasing importance This is particularly true in many cases of meningomyelocele and spina bifida in which fecal and urinary incontinence play a very important role in the social acceptability of the child Fecal incontinence can be managed reasonably satisfactorily by careful bowel control However, in many instances, urinary incontinence presents an insurmountable problem and the usual methods of bladder training and transurethral resection fail in a considerable number of cases Not only are these unfortunates totally unacceptable from a standpoint of urinary odors and skin maceration, but the presence of recurrent urinary tract infections and vesicoureteral reflux adds materially to the problem of their management

In 1955, Smith and Hinman[1] suggested an intussuscepted ileocystostomy for the management of total urinary incontinence This method was used only in animals and was devised to produce continence It has always been our impression that any attempt at continence with the subsequent stagnation of urine and the necessity of repeated catheterization is fundamentally unsound Therefore, we have devised a similar operation except that the ileal segment is anastomosed to the bladder in a peristaltic fashion and the urine collected in a Rutzen bag This operation was undertaken at the suggestion of Dr Carl A Moyer and has proved quite satisfactory in three cases which have been followed for periods of 11, 12, and 15 months respectively, and it is our impression that the procedure has definite merit

OPERATIVE TECHNIQUE

The abdomen is opened through a midline suprapubic incision extending from a point immediately above the symphysis pubis upward and lateral to the left of the umbilicus An isolated ileal segment is established in the customary fashion using a segment of ileum taken approximately 6 cm proximal to the ileocecal valve The length of the segment is dependent upon the size of the individual Routine appendectomy is performed Ileal continuity is re-established by an end-to-end anastomosis using two layers of silk sutures Although the incision into the mesentery must be sufficiently deep to permit free mobility of the segment, considerable caution must be employed to avoid any interference with blood supply to the isolated segment (fig 1, A)

After the segment has been isolated, the peritoneal contents are packed off with gauze and the bladder opened The next step is closure of the vesical neck

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Read at annual meeting of American Urological Association Pittsburgh Pa May 6-9 1957

[1] Smith G I and Hinman F Jr The intussuscepted ileal cystostomy J Urol 73 261–267 1955

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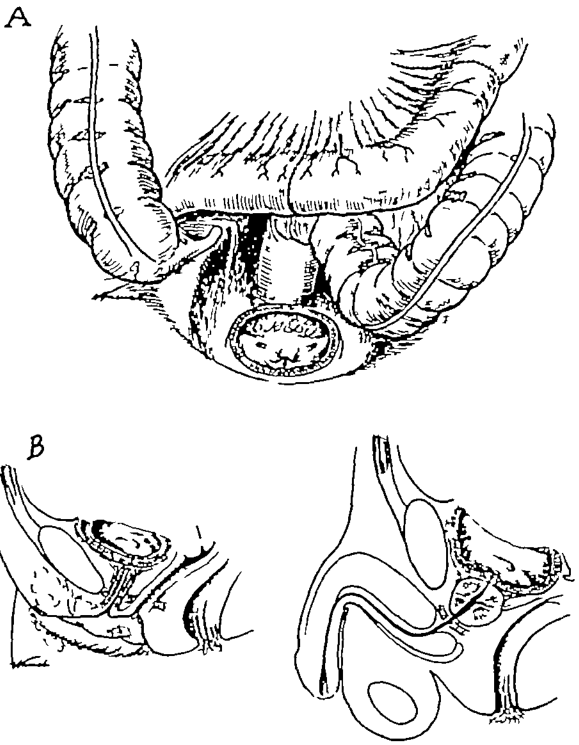

FIG 1

(fig 1, *B*) This may be done extravesically in the female patient, the urethra being severed at the bladder neck and closed with a double layer of 00 chromic catgut sutures, the distal urethra being closed separately In the male the closure is made transvesically in order to avoid possible interference with ejaculation Care must be exercised to obtain a good closure as there is a surprising tendency for leakage through the urethra unless the closure is well accomplished If the bladder is small in capacity the ileal segment is anastomosed directly to the dome of the bladder, an opening being made approximately the circumference as the proximal end of the ileal segment If, however, as is often the case, there is marked flabbiness of the detrusor musculature, the excess bladder is removed and the anastomosis made between the remaining bladder and the ileal segment (fig 2, *A*) Failure to excise a sufficient amount of bladder results in persistent residual urine, as was encountered in case 2 of our series, to be discussed Anastomosis between the ileal segment and the bladder is accomplished by a double layer of sutures, the innermost being 00 chromic catgut with an outer layer of silk Care must be taken that the silk sutures do not penetrate the lumen of either the ileal segment or the bladder as incrustations may develop The bladder may be drained by means of a cystostomy placed through a stab wound prior to completion of the vesicoileal anastomosis or by a urethral catheter passed through the segment The segment is brought out to the abdominal wall at a point midway between the anterior-superior spine of the ilium and the umbilicus and anastomosed to the skin in the fashion utilized in ordinary ileal segment diver-

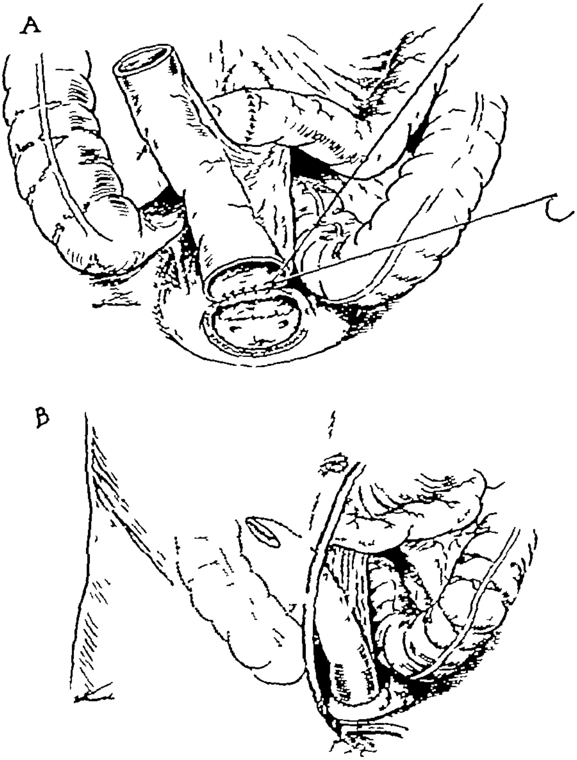

FIG 2

sion (fig 2, *B*) On about the tenth day an ileocystogram is made through the suprapubic catheter and if the anastomosis is intact the suprapubic tube or catheter is removed

CASE REPORTS

T L was seen at the age of 22 months with the history of having had recurrent bouts of fever for one year In addition, he had had progressive difficulty in walking He had also a history of two episodes of urinary retention with incontinence in the intervals between On December 16, 1954, examination revealed 60 cc residual urine, and intravenous pyelograms showed bilateral hydronephrosis and hydroureter more marked on the left (fig 3, *A*) At operation, the neurosurgical service found a meningomyelocele accompanied by a lipomatous tumor involving the sacral cord Postoperative convalescence was complicated by complete urinary retention which failed to respond Several attempts were made at catheter removal, but the child continued to carry a residual urine of 60–75 cc, and have recurrent bouts of fever, and on December 30, a cystogram was made which showed a large dilated bladder with marked hydronephrosis and hydroureter on the right with vesicoureteral reflux (fig 3, *B*) A delayed cystogram showed reflux up the left ureter as well, with hydronephrosis and hydroureter (fig 3, *C*) On January 20, 1955, an ileal segment and excision of a

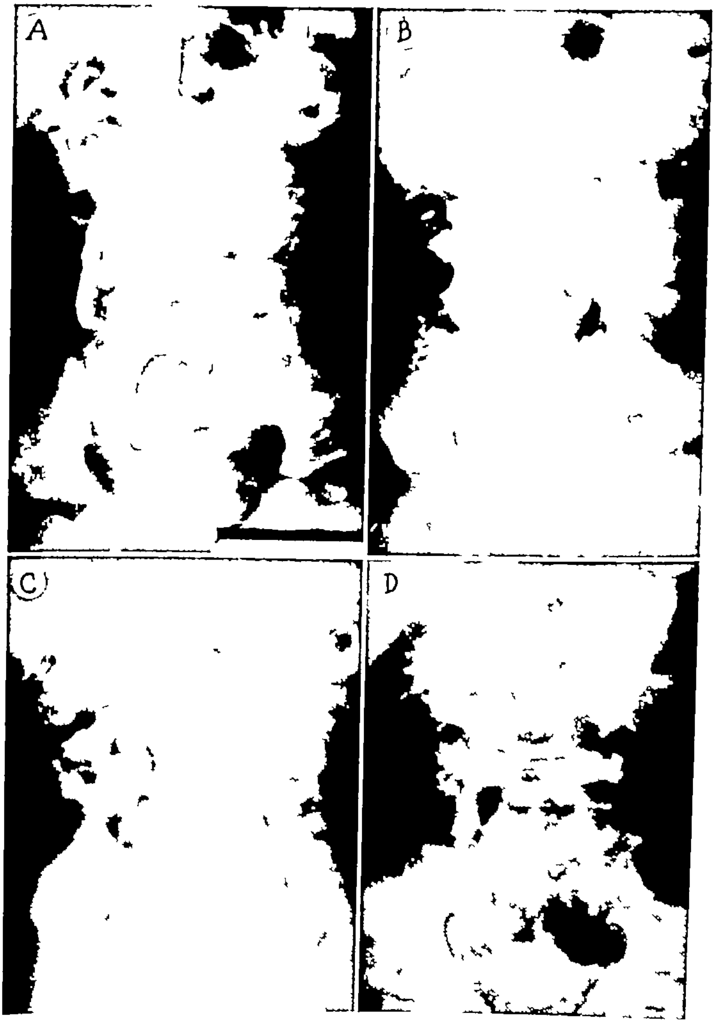

Fig 3

portion of the distended bladder were accomplished The vesical neck was closed intravesically Postoperative convalescence was uneventful The mother could not adapt the patient readily to a Rutzen bag so he wore diapers for a period After about three months a small Rutzen bag was obtained and the mother has been able to manage urine collection quite satisfactorily for the past eight or nine months The ileal stoma has remained well open On examination eleven months postoperatively, the ileal segment contained only 4–5 cc grossly clear urine Intravenous pyelograms showed excellent bilateral function with a complete disappearance of the hydronephrosis and hydroureter (fig 3, *D*) He has continued to grow satisfactorily The complete absence of urinary infection in a patient who formerly had repeated bouts is quite notable

K B was admitted to the Children's Hospital on January 11, 1955 at the age of four years Urinary incontinence was present since birth He had a spina bifida with an arrested hydrocephalus and club feet Operation for closure of the meningomyelocele was performed at age 2 months Urinary sepsis had not been present and intravenous pyelograms were essentially normal Cystogram revealed no reflux The residual urine was 90–100 cc Cystoscopy revealed a marked relaxation of the vesical detrusor and also a wide open bladder neck It was not deemed feasible to perform a transurethral resection because no resectable tissue could be seen After consultation with members of the neurosurgical service, who felt that no possible improvement in the neurogenic situation could be contemplated, an ileocystostomy was decided upon because of the incontinence On January 22, an intravesical closure of the bladder neck was performed and an ileal segment connected to the dome of the bladder Although the bladder was fairly large, no bladder tissue was removed The boy experienced a fairly stormy postoperative course, principal complications being those of ileus and fecal impaction However, he responded satisfactorily and was discharged from the hospital in good condition Very soon after he was discharged he began to pass urine per urethram and on March 30, was readmitted to the Children's Hospital with practically all of the urine coming through the urethra Catheterization of the ileal stoma revealed 45 cc very cloudy urine in the bladder On April 2, at a second operation the bladder neck was re-closed, about two-thirds of the remaining bladder excised, and the ileal segment reanastomosed to the base of the bladder Convalescence was essentially as before, however, the child did reasonably well and since discharge from the hospital has done remarkably well The ileal segment is now empty on catheterization He has had no urinary sepsis and the intravenous pyelograms have remained normal

W D was first seen at the Children's Hospital on August 6, 1952, at the age of 10 days with an infected meningomyelocele of the lumbar spine The prognosis was considered hopeless However, she responded well to chemotherapy and a repair of the meningomyelocele was performed on June 6, 1953 Early in life she presented a progressive hydrocephalus which became arrested spontaneously In

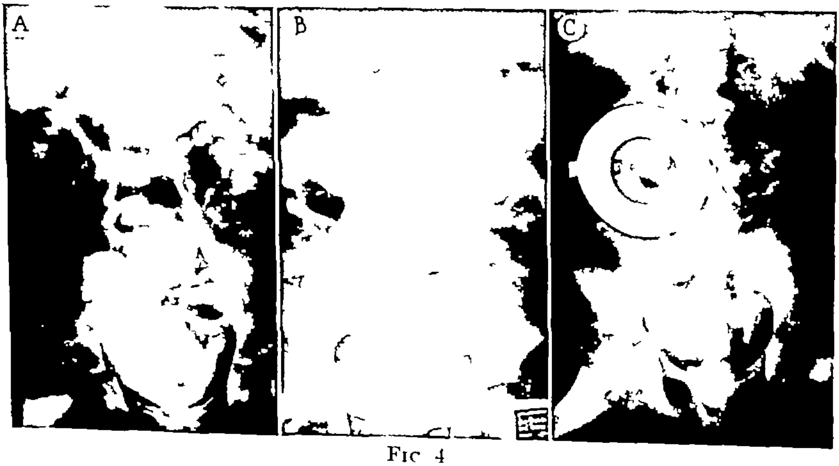

Fig 4

addition, she had paralysis of both legs At all times she was found to have a markedly hypotonic bladder with total urinary incontinence She was seen by the urology service for the first time on July 30, 1955 with a history of chronic urinary tract infection for a period of six months, and residual urine of 65 cc In January 1955, intravenous pyelograms had been reported normal However, on July 30 a cystogram revealed reflux up the left ureter with marked hydroureter and hydronephrosis (fig 4, *A*) On cystoscopy a heavily trabeculated bladder was noted with marked relaxation of the bladder neck Intravenous pyelograms showed moderate bilateral ureterectasis, but the dilatation was not as striking as that noted in the cystogram (fig 4, *B*) Infection persisted in spite of antibiotic therapy On September 19, an ileocystostomy was performed with excision of a considerable portion of the bladder and closure of the bladder neck Convalescence was uncomplicated Intravenous pyelograms one month postoperatively showed definite improvement in the ureteral dilatation with good bilateral function Convalescence since that time has been completely uneventful and on September 1, 1956, the stoma was noted to be good, the urine clear, the segment completely empty She was eating well and gaining weight Intravenous pyelograms one year later showed excellent bilateral function and demonstrated rapid filling of the ileal segment (fig 4, *C*)

DISCUSSION

Because of the permanent nature of this operation, we believe that it should be reserved for those cases of extensive neurologic involvement of the detrusor musculature of the bladder, accompanied by urinary incontinence, in which other methods of management have failed The presence of persistent urinary tract infection with progressive upper tract damage is also an indication for definitive surgery The operation as described is not an unusually difficult technical procedure The necessity for suprapubic tubes, with accompanying persistent infection and frequent changes of tube, is completely eliminated Peristaltic activity of the segment eliminates stagnation of urine and vesicoureteral reflux is no problem It is our impression that this operation is superior to any other type of urinary diversion in the cases herein described The operation should also be applicable to any case in which malignancy is not a problem if the ureters and ureterovesical mechanism are not obstructed, for example, extensive urethral scarring with multiple perineal fistulas

SUMMARY

A method of urinary diversion utilizing an isolated ileal segment and a portion of the bladder is presented This procedure has been used successfully in three cases of meningomyelocele

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AN EVALUATION OF VESICOURETERAL PLASTY FOR REFLUX

CLIFFORD E. VINSON, JOHN A. HUTCH AND R. CARL BUNTS

From the Urological Section, Surgical Service, McGuire Veterans Administration Hospital, Richmond, Va.

Vesicoureteral reflux with its sequelae of hydroureter, hydronephrosis, retrograde infection and renal insufficiency has been the most formidable urological complication encountered by us in the treatment of 1000 paraplegics. Final urologic rehabilitation of the paraplegic cannot be considered to be complete until the patient no longer requires catheter drainage. This cannot be accomplished if the patient has irreversible vesicoureteral reflux.

Morales, Sullivan and Hotchkiss in studying renal function in paraplegics have shown that reflux is a major factor in the cause of renal insufficiency. Emmett and Simon in treating 158 patients with urological complications from myelodysplasia and congenital bladder neck obstruction found that ureteral reflux was the factor that so often defeated the efforts of treatment by transurethral resection of the bladder neck.

After several unsuccessful attempts to alleviate reflux by simple reimplantation of the ureter, an operative procedure was devised by one of us (Hutch) which has three principles. First, the attachment of the ureter to the trigone is preserved, second, a long intravesical ureter is constructed, and third the bladder wall behind the ureter is reinforced.

This procedure has subsequently been used by us and others for the elimination of reflux due to other etiologic factors. It has now been in general use for the past 7 years and it was thought advisable to re-evaluate the results of the procedure.

A questionnaire was mailed to several hundred urologists throughout the United States in which we inquired as to the number of procedures performed, and the percentage of success or failure in reflux associated with or resulting from the following conditions:

Structural or neurogenic, as observed in the patient suffering cord injury or disease. It is our opinion that reflux in these patients is the result of anatomical changes in or near the vesicoureteral opening. These changes are indirectly associated with cord injury and probably result from erratic nerve impulses originating in the distal stump of the cord, causing the bladder to become trabeculated and contracted. The complications that accompany cord injury such as bladder stones, prolonged cystitis and the ever present foreign body (catheter or suprapubic tube) are probably also factors in the development of reflux in the paraplegic.

Neurogenic, due either to a congenital malformation or a myelodysplasia of the central nervous system as seen in spina bifida, meningocele, etc. The bladder in these patients, in most instances, has been found to be heavily trabeculated

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Read at annual meeting of Mid Atlantic Section of American Urological Association, Virginia Beach, Va., March 21-24, 1957.

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with cellule formation and although some may have a hypotonic bladder, the majority have hypertonia.

Obstructive, observed in congenital bladder neck obstruction, urethral valves, etc. Inspection of the bladder in these patients shows the same anatomical changes noted in the cord injury patient but to a less degree.

Idiopathic. This group includes those without demonstrable obstruction or changes as noted in the bladder of those described above. Cystometric studies have shown a slight increased tonicity and greatly increased capacity. The aparasympathetic bladder, as recently described by Swenson, with megalobladder and megaloureter with or without reflux, make up the majority of patients in this category. Also there are a number who have been classified as idiopathic and after very careful study, will be found to be on an obstructive or other etiologic basis.

Miscellaneous. Under this heading, for tabulation purposes, we have placed the patients in whom the reflux was associated with congenital anomalies of the vesicoureteral junction such as diverticulum, ureterocele and the ureter in exstrophy of the bladder. The rare patient who has an acquired reflux following injury of the ureteral meatus due to resection of tumors overlying the meatus, prostatic resection, and rarely following ureteral meatotomy is considered in this miscellaneous category.

We have found it necessary for statistical purposes to list 12 operative procedures in a separate unclassified category, inasmuch as the respective etiologic agents of the reflux were not stated on the returned questionnaires.

RESULTS OF SURVEY

Replies were received from 232 urologists. Fifty had performed vesicoureteral plasty 169 times in 89 patients. Fifty-nine stated that they had used some other surgical procedure in treating vesicoureteral reflux, such as nephrostomy, nephrectomy if unilateral, cystostomy, and transurethral resection for removal of obstructing tissue. Those who directly attacked the vesicoureteral junction used several procedures such as reimplantation either by the cuff method, "fish mouthing" of ureter or oblique pull-through with mucosa-to-mucosa anastomosis. A very small percentage did not use any procedure for correction of reflux inasmuch as they were of the opinion that reflux was not detrimental. Some believe that reflux will invariably disappear if the obstruction is removed.

The questionnaire was made as simple as possible and allowed no opportunity of interpretation on our part. The criteria for a good result were first, no reflux present, second, same or improved pyelograms, and third, clinical improvement. If the repair failed, the cause of the failure was noted.

Of the 169 ureters in which repair was carried out as reported by the respondents, 119 or 70 per cent were successful (table 1), of 83 vesicoureteral plastys performed by the authors and their associates (residents) 66 or 79 per cent were considered to be successful (table 2). As shown, the over-all statistics of the respondents closely correspond with the experience of the authors. Two Eastern clinics who reported 22 failures in 25 plastys accounted for over one-third of the failures of the 50 respondents. Table 3 gives the combined results

TABLE 1 *Results of survey*

Etiology	Patients	Ureters	Success	Failure
Structural and neurogenic	20	22	20 (91%)	2 (9%)
Neurogenic (myelodysplasia)	6	9	6 (67%)	3 (33%)
Obstructive	60	83	58 (70%)	25 (30%)
Idiopathic	27	38	30 (84%)	8 (16%)
Miscellaneous	5	5	5 (100%)	0 (0%)
Unclassified	7	12	0 (0%)	12 (100%)
Totals	89	169	119 (70%)	50 (30%)

TABLE 2—*Authors' results*

Etiology	Patients	Ureters	Success	Failure
Structural and neurogenic	38	60	45 (75%)	15 (25%)
Neurogenic (myelodysplasia)	5	8	6 (75%)	2 (25%)
Obstructive	2	2	2 (100%)	0 (0%)
Idiopathic	8	13	13 (100%)	0 (0%)
Totals	53	83	66 (79%)	17 (21%)

TABLE 3 *Combined results*

Etiology	Patients	Ureters	Success	Failure
Structural and neurogenic	58	82	65 (79%)	17 (23%)
Neurogenic (myelodysplasia)	11	17	12 (71%)	5 (29%)
Obstructive	62	85	60 (72%)	25 (28%)
Idiopathic	35	51	43 (84%)	8 (16%)
Miscellaneous	5	5	5 (100%)	0 (0%)
Unclassified	7	12	0 (0%)	12 (100%)
Totals	178	252	185 (74%)	67 (26%)

There was one death in the authors' series that occurred five days postoperatively due to a fulminating pyelonephritis No deaths were reported in the survey

Analysis of failures On analyzing the failures from the survey and in our patients it was found that all were due to either a recurrence of the reflux or obstruction Twenty-nine (58 per cent) patients as reported in the survey and 12 (70 per cent) of our series had a recurrence of reflux, while 21 (42 per cent) and five (30 per cent), in order, acquired obstruction

We have found that the recurrence of reflux in our patients has occurred immediately (seven ureters) following repair or several months afterwards (five ureters) On cystoscopic inspection of the patient in which recurrence is immediate, it is noted that the ureter has retracted to its original bed (fig 1) We believe this may be due to faulty technique at the time of the operative procedure and may result from incomplete mobilization of the lower one-third of the ureter The ureter should be dissected free so that it may adjust to its new with cellule formation and although some may have a hypotonic bladder, the majority have hypertonia

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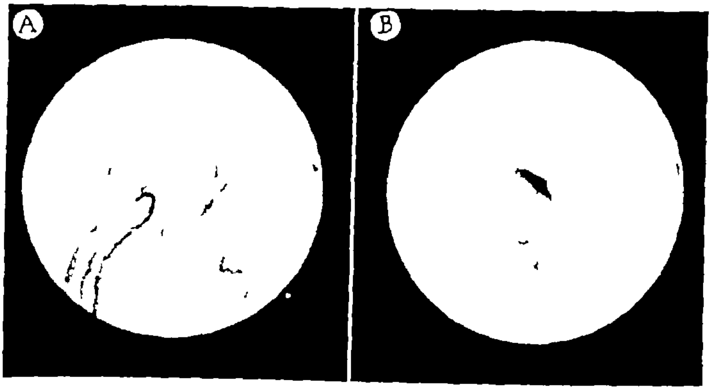

FIG 1 *A*, cystoscopic appearance of successful ureteral plasty *B*, failure, ureter retracted

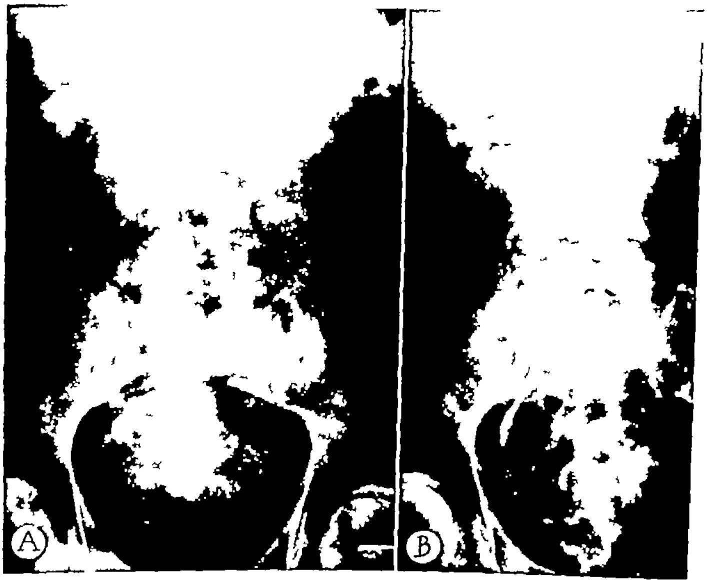

FIG 2 Excretory urograms (30 minutes) Pre and post subarachnoid alcohol injection

course through the bladder wall without tension and will not retract to its former position

In those patients who have a delayed recurrence, we feel that there has been a failure to eliminate the factors which caused the reflux In support of this hypothesis is the development of reflux on the normal side in five cord injury patients who previously had had repair of an unilateral reflux Hydroureter and nephrosis and early reflux have been shown to decrease and, in some instances, disappear in the cord injury patient who has had the sacral reflex arc eliminated Figure 2 shows the excretory urogram of a patient whose left kidney had been destroyed by late recurrence of reflux Hydroureter, hydronephrosis, and partial reflux developed in his remaining kidney Following this, subarachnoid alcohol injection destroyed the sacral reflex centers reducing the spasticity and hypertonicity of the bladder with a subsequent disappearance of the reflux, hydroureter, and hydronephrosis Patients who had a postoperative recurrence of reflux, although not benefited, were not harmed by the operation

Obstruction, by far the more serious complication, may be partial and temporary, as seen in three ureters of our series We attribute this temporary obstruction to postoperative edema or tight suturing around the ureter at its exit from the bladder Permanent ureteral obstruction may vary from a slight increase in dilatation of the lower ureter to complete obstruction In analyzing our patients in whom permanent obstruction has developed, we believe that the ureter was not allowed to pass through the bladder wall loosely and without tension or angulation over the area from which it was dissected Acute angulation results from tight suturing beneath the intravesical ureter near its exit combined with improper fixation sutures, as depicted in fig 3

In one of our patients and another reported in the survey, an interureteric fibrous band formed between the newly created intravesical ureters producing an acute medial angulation (fig 4) Resection of this band resulted in the immediate retraction of the nipples to a lateral position, thus relieving the obstruction

Another cause of obstruction noted by us is the escape of urine around the ureter or into the sheath of the partially denuded ureter (fig 5) This has resulted in fibrosis of the ureter with gradual compression and final obstruction

The procedure used by us has the added advantage that reoperation is possible since the ureter has not been shortened by previous surgery Nephrectomy has been necessary in only one patient, as reported in this survey A majority of the patients had reimplantation by the cuff or other methods In several, nephrostomy was necessary to preserve the function of the involved kidney

Comment There is no more controversial subject in urology today than that of vesicoureteral reflux There are still some who believe that vesicoureteral reflux is of no consequence, but those of us who must care for a large number

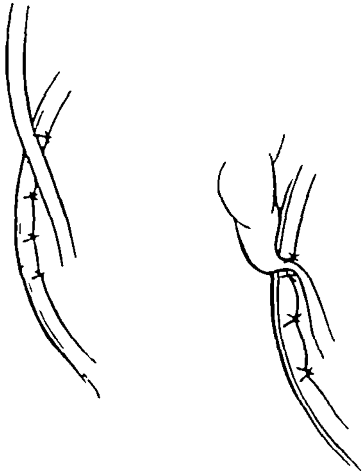

FIG 3 Angulation of ureter as result of improper suturing

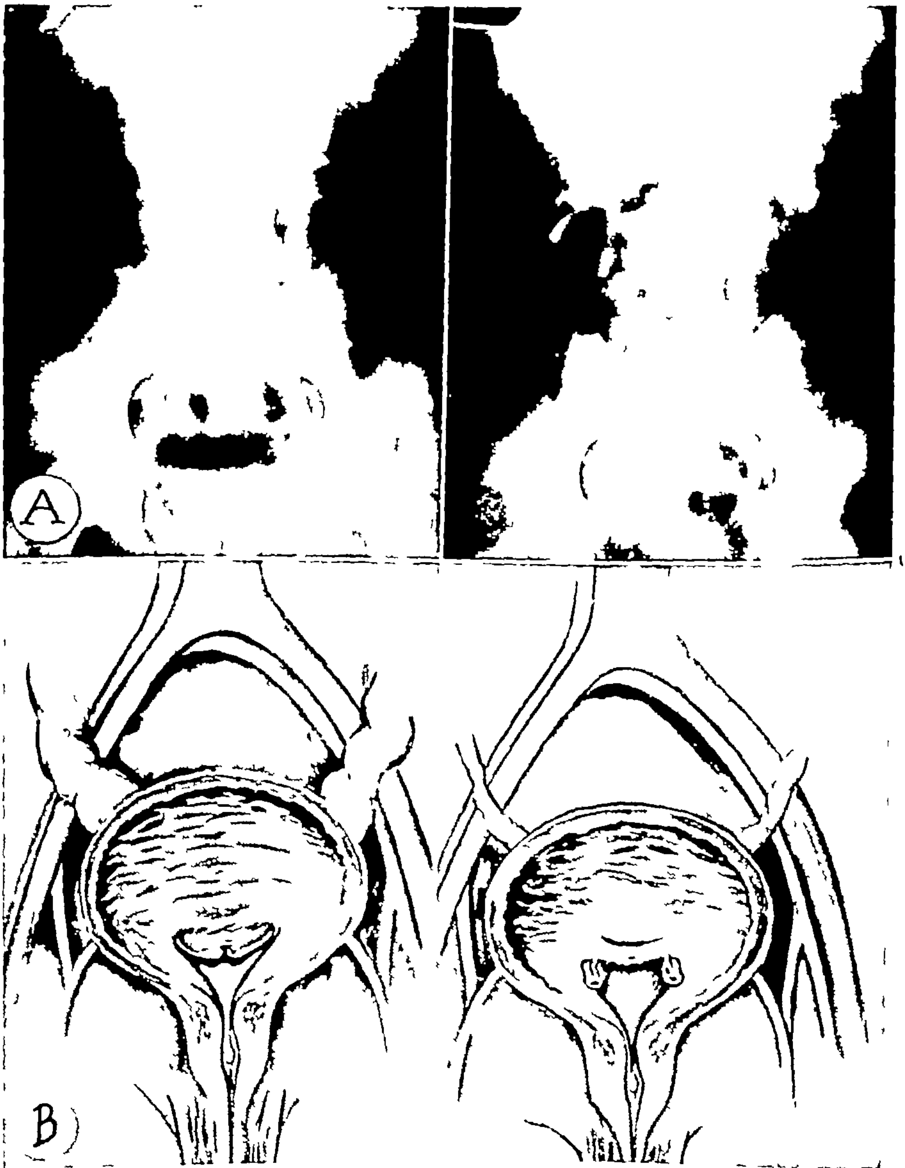

FIG. 4. Medial angulation of ureter due to fibrous band. A, 30 minute excretory urogram. B, cystoscopic appearance pre and post resection of band.

of these patients are convinced that it is a major cause of renal insufficiency. Emmett, in describing the consequences of persistent reflux states, 'Its presence appears to increase the degree of ureteral dilatation, as well as the rate at which pyeloureterectasis progresses. Furthermore, it may be the complicating factor that allows renal insufficiency to progress to fatal termination even after operation on the vesical neck has eliminated residual urine and restored normal or near normal vesical function."

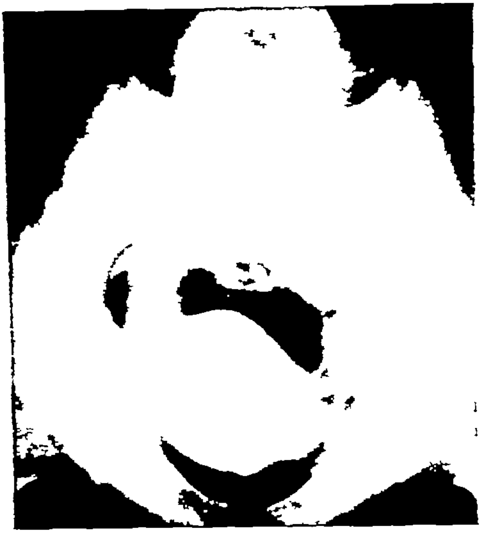

FIG 5 Cystogram demonstrates extravesical leakage of contrast material around repaired left ureter

We are becoming increasingly convinced that reflux in the majority of patients will be found in most instances in the patient with a hypertonic bladder in which there is a sustained tonus with anatomical changes such as coarse trabeculations, cellules and diverticulum formation in or near the intramural ureter

This is substantiated in part by our operative results in which there has been no recurrence of reflux in the idiopathic group although the majority of these bladders are hypertonic or in five ureters repaired in the miscellaneous group In these patients the bladder wall and mucous membrane were normal Seven patients with hydroureter and hydronephrosis without reflux but with a physiologic narrowing of the intramural ureter were successfully treated by vesicoureteral plasty Hutch and others feel that the same forces are at work in these patients namely anatomical changes in or near the intramural ureter

It is our opinion that although we may better our over-all results by improving our surgical technique we will never achieve perfect results unless we eliminate the primary cause of reflux. We believe that this may be accomplished in selected paraplegic patients by converting an upper motor neuron hypertonic bladder into a lower motor neuron hypotonic bladder by destruction of the sacral reflex centers This may be accomplished by rhizotomy conectomy sacral neurectomy or subarachnoid alcohol injection Vesicoureteral plasty will only then be necessary when the reflux has become irreversible Reflux if not irreversible may be eliminated in the patient with congenital bladder neck obstruction myelodysplasia and in many with reflux of idiopathic etiology by enlargement of the bladder orifice by transurethral resection or Y-plasty In the patient with irreversible reflux Y-plasty of the anterior bladder neck may be combined with ureteral plasty One respondent reported the use of this technique in the surgical repair of reflux with success in 14 of 15 ureters

We do not feel that our type, or for that matter, any type of plastic repair in itself, will result in the *correction of reflux in the tremendously dilated, atonic and* tortuous ureters with loss of renal function These patients in most instances will require a series of procedures first, nephrostomy drainage with lysis and straightening of kinks of the upper ureter, followed by bladder neck widening, vesico ureteral plasty, and lysis of adhesions of the lower one-third of the ureter Also, we do not aver that our procedure should be used in preference to all others Vesicoureteral plasty is controversial and as an operative procedure is still in its infancy Possibly, in the future, if we are able to determine the precise pathogenesis and are successful in eliminating the cause of reflux in its incipiency, all *operative techniques in this area will be successful*

SUMMARY AND CONCLUSIONS

Vesicoureteral plasty for reflux, found in patients with cord injury or disease, myelodysplasia of the central nervous system and peripheral nerves, congenital bladder neck obstruction, idiopathic, and congenital and acquired conditions, has been performed by 52 individual urologists or clinics on 178 patients and 252 ureters of which 185, or 74 per cent, were successful

Success was most often encountered in those patients who had a normal or near normal appearing bladder wall

Complications were those of a recurrence of the reflux or obstruction of the ureter at the operative site The causes and methods of prevention of these complications are discussed

The technique of vesicoureteral plasty employed in this group of patients affords the advantage of a correction of the most serious complication, obstruction

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FRACTURE OF THE PENIS: TRAUMATIC RUPTURE OF CORPORA CAVERNOSA

A. A. CREECY AND F. S. BEAZLIE, JR.

Fracture of the penis is properly defined as rupture of the corpora cavernosa occurring when the penis is in erection. It is rare in both civilian and military life. Young found only 43 cases of penile injury in American Forces in World War I, and Marshall reported only 18 genital injuries in 8,310 casualties of which only two were of the penis alone and 10, penis and testis. Fetter and Gartman found only 10 reported cases from 1926 to 1935, and stated that at Jefferson Hospital, Philadelphia only one case had been examined from January 1, 1916, to November 1, 1935, an incidence of 1:175,000 admissions. No cases appeared in the American literature after 1936 until that of Thompson in 1954. Table 1 gives all the cases that could be found from an extensive search of the "modern" world literature, a total of 19 cases including the three reported here.

The etiology in these cases was most often a direct blow to, or bending of the erect penis, and less often *faux pas de coit*. Four occurred by rolling over in bed, six by striking or kneading with the hand to reduce the erection, one by bumping into a chair, one by being thrown against the knob of the saddle on a motorcycle, one by striking the toilet seat, one by a *coup de pied* in a fight, one presumably by the kick of a horse, and four during coitus. Fifteen cases out of 19 were due to various types trauma other than coitus.

By contrast, in an older series made up of authors quoted by Malis, Mende had collected 15 cases in which nine were due to coitus. Hyrtl had collected four cases, two due to coitus, one to masturbation, one to hitting a bedpost, and five other cases of individual authors not due to coitus, a total of 24 cases in which coitus was the etiological agent in 11 and other trauma in 13. Combining both series for a total of 43 cases, trauma is the cause in 28 and coitus in 15.

The characteristic pathology of the lesion is a tear in the tunica albuginea of the corpora cavernosa with hemorrhage, hematoma formation and distortion of the organ. If the urethra is also ruptured, the injury is much more severe. In either case, the penis becomes markedly swollen, discolored, and bends away from the injured side. Extravasation of blood and/or urine along the fascial planes into the scrotum and perineum and even into the lower abdomen and thighs may occur and complicate treatment. Two factors may predispose to the rupture: 1) the thinning out of the tunica albuginea which occurs during erection, and 2) previous periurethral infection. In Mende's cases, eight out of 15 cases were complicated by urethral injury also, and Malis states that in 18 cases described by Bramann, 10 had rupture of the urethra. In the "modern" series above, only three cases were complicated by urethral injury.

The victim of such a catastrophe often recalls hearing a cracking sound followed by collapse of the erection, pain which may be severe and occasionally

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Read at annual meeting of Mid Atlantic Section of American Urological Association, Virginia Beach, Va., March 21–24, 1957.

TABLE 1

Author	Year	Age Pat	Etiology	Delay	Treatment	Duration in Hospital	Result
Mahs	1924	54	Hand to reduce erec	24 hr	Warm compresses	14 days	No deform Normal funct
Frankenthal	1925	29	Thrown on saddlehorn motorcycle	24 hr	Perineal repair of urethra over cath and drainage	16 days	No deform Normal funct
Redi	1926	20	Rolled over in bed	0	Ice and compresses	11 days	No deform Normal funct
Sommer 2 cases	1926	40	Hand to reduce erec	48 hr	I&D of c c with primary suture of tunica albuginea	14 days	No deform Normal funct
	1926	22	Hand to reduce erec	0		14 days	
Sinkoe	1931	30	Hit against stool	0	Cold compresses	10 days	No deform Normal funct
Blanc and Duroselle	1932	25	*Coup de pied*	96 hr	I&D of c c and excision of cyst	16 days	No deform Normal funct
Baretz	1932	35	Rolled over bed	0	Cold compresses	10 days	No deform Normal funct
Konecny	1933	52	Struck with hand	72 hr	Gangrenous gland amputated, urethroplasty	? weeks	Deformed ? function
McKay and Hawes	1935	30	Rolled over in bed	0	Compresses	10 days	Normal function
Fetter and Gartman	1936	48	Caught in p j —hit with hand	24 hr	Compresses 8 days as o p —fol by hosp and evac of clots & suture of c c	21 days	Normal function
Rummelhardt 3 cases	1953	?	Coitus	?	1 with compresses 2 with I & D of c c	8–14 days	Normal function
		?	Coitus	?			Normal function
			Hit bedp				Normal function

TABLE 1—*Continued*

Author	Year	Age Pat	Etiology	Delay	Treatment	Duration in Hospital	Result
Thompson	1951	38	Kicked by horse ?	24 hr	Catheter & compr Evac of clots	16 days	Angled pain on erect
Iurmin	1954	34	Kneaded penis to break erec	1 hr	Cold compresses Infra red rays	14 days	Normal function
Haak and Warden	1955	35	Rolled over in bed	24 hr	Ice bag & elev	4 days	Normal function
Rosenthal and Rosenthal	1955	54	Coitus, penis rammed mattress	0	Foley catheter	22 days	Norm funct 2 mon nodef
Creecy and Beazlie	1956	43	Coitus	0	Cystostomy & I & D of c c —Perineal urethrotomy suture of urethra over cath and suture of T A also trypsin	71 days	Norm funct 2 mon nodef

accompanied by shock, and then notes the bizarre swelling, discoloration and distortion of the organ The patient may urinate with difficulty or not at all Hematuria is present with urethral injury He may delay seeking medical help and offer a vague history, but usually inspection of a pale, apprehensive person and his swollen, distorted organ makes the diagnosis apparent

All the authors agree that treatment should be conservative The cases without a urethral tear have usually been handled by inserting an indwelling catheter, using a compress bandage, and cold application Later, the hematoma may have to be evacuated In cases with urethral injury, in which catheterization is impossible, cystotomy with retrograde urethral catheterization or cystostomy may be be done We believe that the use of the enzyme, trypsin, intramuscularly is a valuable adjunct in hastening resolution of the ecchymosis and extravasation which occur in these cases, as well as in cases of urinary extravasation due to other causes in which we have used it Varidase may serve the same purpose

Most of the authors state that the prognosis should be guarded, and in talking to physicians, including many urologists, it is commonly assumed that impotency and difficulty will be the aftermath of such injury However, in all of the cases reported in detail, return of erections and ability to have coitus have been excellent Only in a few cases has there been some residual deformity, but this has not been sufficient to prevent function

CASE REPORTS

Case 1 (Haak and Warden) A O S , 35-year-old white man, was admitted to the Washington County Hospital, Hagerstown Maryland January 18, 1955, stating that on the previous day when he awoke he had a vigorous erection Inadvertently he rolled over in bed and suddenly noticed severe pain in his penis Self-examination revealed swelling and discoloration of the shaft of the penis He stated that following this he was able to empty his bladder without difficulty The swelling increased until admission

Physical examination was essentially negative except for the genitalia The penis was enlarged edematous and generally ecchymotic

The patient was treated conservatively by support of the genitalia and by ice packs He was discharged four days later for care at home Subsequently the shaft of the penis reduced to normal size and the ecchymosis disappeared

Two months later inquiry revealed that upon erection he had no angulation of his penis

Case 2 (Rosenthal and Rosenthal) R P W , 67-year-old-minister, was admitted to the Virginia Baptist Hospital on September 10, 1955 with the history that while having intercourse his penis slipped and struck the bed, then he began to bleed profusely with a moderate amount of penile pain He noticed that the penis became swollen particularly on the right, but gradually spread and involved the prepuce and shaft

Examination on admission revealed only the positive findings enumerated here The penis was quite swollen, tender and ecchymotic, and the prepuce edematous Moderate bleeding occurred from the urethral meatus The diagnosis was fracture of the penis with a urethral tear Fortunately, the patient had had no desire to void and a No 18 5 cc Foley bag catheter passed into the bladder with ease He was left on catheter drainage for eight days and although the penis was somewhat swollen and ecchymotic, he voided with ease The following day however, he returned with profuse hemorrhage from the urethra and a No 18 Foley bag catheter was reinserted and left indwelling On that occasion a catheter

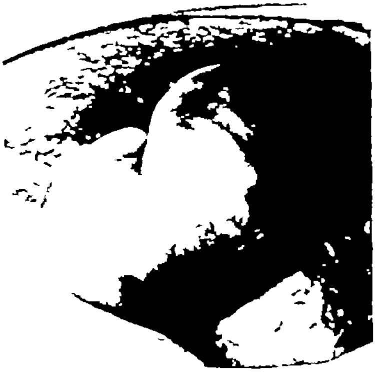

FIG 1 Initial injury fracture of penis

was left in place 14 days Following its removal the patient had no further difficulty, the swelling and ecchymosis had disappeared and he felt quite well He has denied that there has been any loss of libido, he denies any impotence or change of any type in his sexual condition

Case 3 (Creecy and Beazlie) W W S, No 154070, a 43-year-old white bus driver, was seen on January 15, 1956 He said that one hour prior to admission he was having coitus with his wife, she in the supine position and he in the prone position, when suddenly he noted pain in the penis and felt that something was wrong He denied hearing any sound, but upon examining the penis, saw that it was swollen and discolored He tried to urinate but could not and therefore went to his physician, Dr William Goldsmith who called us to see him Examination disclosed that the penis was markedly swollen and angulated to the right in a semicircle It was a dusky, brownish-red color having the appearance of a liver sausage (fig 1) He was uncircumcised The scrotum was swollen and purplish The penis and scrotum were tense to palpation, and tender A catheter would not pass into the bladder and met an obstruction in the deep pendulous urethra

A diagnosis of rupture of the penis was made and the patient taken to surgery Lateral incisions were made on each side of the shaft of the penis and a considerable amount of clotted blood evacuated A dorsal slit was made to expose the glans The corpora could not be cleanly identified because of the effusion of blood into the tissues with swelling and discoloration Further efforts were made to pass a urethral catheter, but it came through a hole in the urethra anterior to the triangular ligament on the left, and the passageway from here into the bladder could not be found with the amount of swelling and bleeding present Therefore, suprapubic cystostomy was done and a compression bandage applied to the penis

Postoperatively, he was given chloromycetin and trypsin for nine days The ecchymosis subsided within four days, but some swelling persisted By January 29, 1956 the penis had healed and perineal urethrotomy was accomplished A

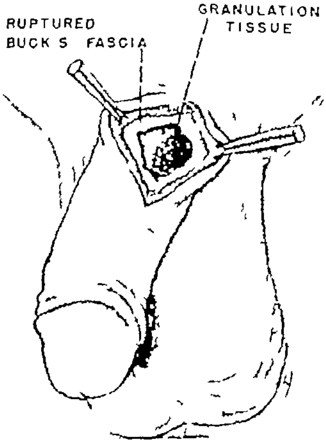

FIG 2

18F Foley catheter was inserted through the urethra and guided into the bladder through the perineal wound It was believed that the urethra would heal over the catheter The suprapubic tube was left in place and worked well The urethral catheter functioned well until February 6 when it became occluded and was changed without difficulty It contined to work well until February 19 when it again became obstructed and was replaced with a 20F Foley catheter On February 23 the urethral catheter was removed The patient voided several hours later and it was noted that the penis became slightly swollen and crepitant on palpation Warm soaks were applied to the penis and since the suprapubic tube was still in place, he was given an additional period of time for healing to occur The penis returned to normal size and shape but each time the suprapubic tube was clamped off and the patient voided swelling of the penis would reoccur Therefore, on February 28 the patient was taken to surgery again A lateral incision was made along the left corpus cavernosum extending from the symphysis pubis almost to the glans The subcutaneous tissue was easily freed up posteriorally from Buck's fascia and the edge of a large rent in Buck's fascia was seen (fig 2) The subcutaneous tissue was then dissected free from Buck's fascia for approximately half the circumference of the penis exposing a large, jagged rent in the fascia This was triangular in shape and approximately 2½ cm in length along the sides of the triangle The base was toward the triangular ligament Upon lifting up this triangular flap, a defect could be seen in the corpora and a hole in the urethra approximately 4 mm in diameter was observed (fig 3) The urethra was closed over a catheter (fig 4) The rent in Buck's fascia was closed (fig 5), the subcutaneous tissue loosely approximated and the skin closed

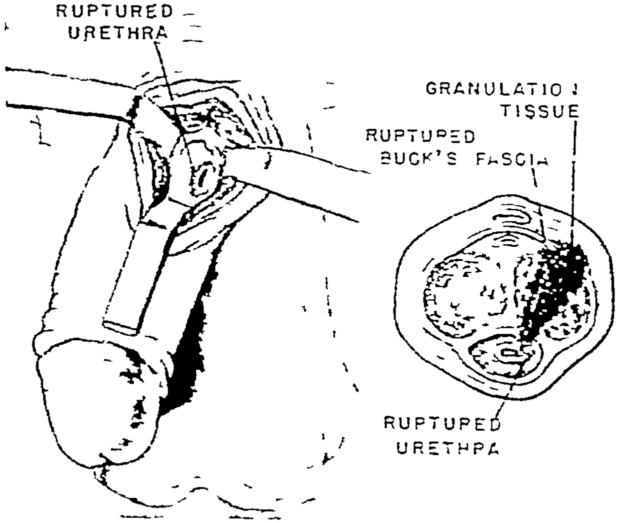

Fig 3

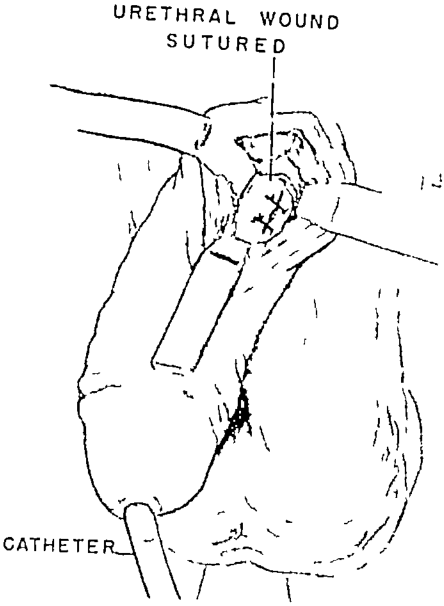

Fig 4

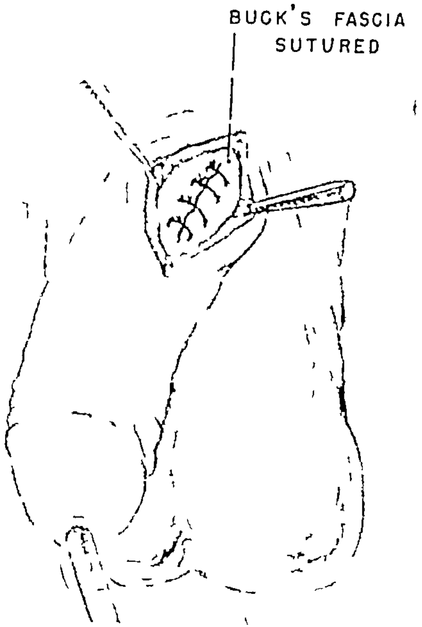

Fig 5 Final result Operative scars

Fig 6

Fig 7

over all From here on the patient's convalescense was smooth and uninterrupted The skin sutures were removed from the penis on the seventh postoperative day, the urethral catheter was removed on March 20, and when the suprapubic tube was clamped the patient voided well On March 21 the suprapubic tube was removed The wound healed rapidly The patient continued to urinate without difficulty and was discharged on March 27, 1956 (figs 6 and 7)

The patient was seen in the office on April 2, 1956 at which time his wounds were well healed, he was able to void a good stream and stated that he was experiencing erections On April 9 he stated that he had an even better stream The accompanying pictures, taken at this time, show complete healing Since then the scars have contracted so as to be hardly noticeable The patient states that he has coitus without difficulty and with no pain or deformity

Addendum Since writing this paper, we have had a communication from Dr J Edward Hill, Richmond, Va who stated that he too had treated a case of fracture of the corpora cavernosa Dr Garnett Link of Petersburg, Va has also reported to us verbally the interesting case of a patient who slammed his penis in a car door Both of these cases responded to conservative treatment Drs O'Heeron, Fish and Boren have illustrated a case of theirs, without description in an article on hematuria in Postgraduate Medicine for July 1956 (vol 20, pp 57–71) Our own patient was last seen in the office on March 4, 1957 at which time he voided an excellent stream He stated that he still had regular, satisfactory sexual relations, although he did state, for the first time, that erections were not so firm as they had been previously

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SCROTAL POUCH TECHNIQUE FOR ORCHIOPEXY

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Some cases of orchiopexy fail because the testis is permitted to lie inside the muscular dartos and cremaster fascia at the end of the operation. Subsequent contractions of the dartos and cremaster during the immediate postoperative period tend to pull the testis back to the external ring, at the top of the scrotum. The spermatic cord then consolidates in a shortened position, during the healing stage, immediately after the operation. The end result is that the testis lies in an unsatisfactory high position. Some surgeons try to overcome this hazard by pushing the fibers of the dartos and cremaster aside, working from within the scrotum, just before the end of the operation. They advise invaginating the bottom of the scrotum into the inguinal wound so that this can be accomplished more easily. Under actual operating conditions it is usually technically difficult, if not impossible, to do a satisfactory job of pushing these layers aside to a sufficient degree. Therefore, since 1947 it has been our practice and teaching at the Squier Clinic to modify Petrivalsky's technique by making a separate transverse incision in the skin of the scrotum, half-way up its wall, and to undermine a pocket between the skin and the dartos, of sufficient size to accommodate the testis and its attached epididymis and tunics (figs. 1–5). In this way we ensure the fact that the testis will be located in a position outside both the dartos and cremaster and will lie immediately under the skin. A traction suture of medium silk is placed through the lower end of the testis and made to come out at the very lowest point of the scrotum, near the midline. Gentle traction is maintained on this suture for a period of 10 days immediately after the operation, by means of an elastic band which is fastened to an adjustable anchor of adhesive tape in the vicinity of the patient's knee. It is important that the traction suture should not come through the auxiliary incision in the scrotum. If it does come through the scrotal incision, the tension of the elastic band will tend to pull the testis out through the incision during the postoperative days. It is for this reason that we bring the traction suture out through a separate point in the skin at least 1 cm. distant from (below) the scrotal incision.

The Torek method also ensures that the testis will lie outside the dartos and cremaster by making a hole completely through all layers of the scrotum, and placing the testis outside the scrotum while it is fastened to the fascia of the thigh. The Torek method has disadvantages, however, such as the necessity for a second operation, and the possibility that excessive rigid traction on the testis during the postoperative period may interfere with its blood supply.

In making the scrotal pouch it is advisable to undermine the skin in all direc-

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Technique presented in Scientific Exhibit at annual meeting of the American Urological Association, Pittsburgh, Pa., May 6–9, 1957.

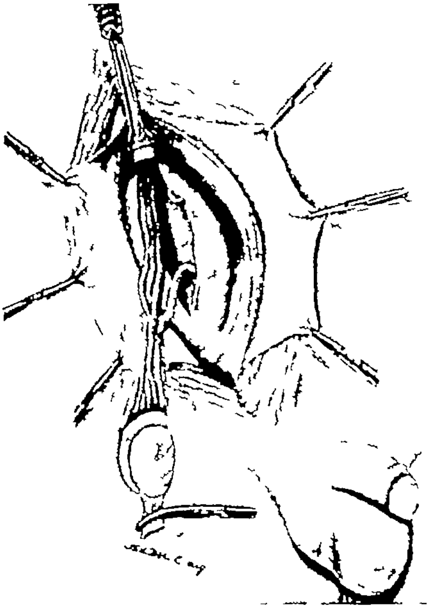

FIG 1 As in any method of orchiopexy, spermatic cord is dissected up beyond internal inguinal ring a sufficient distance to free vessels and ductus deferens from their attachments to hernial sac, posterior peritoneum and body wall When these adhesions are separated and cremaster fascia removed from cord, it is usually possible to achieve a sufficient length of cord to enable testis to reach to bottom of scrotum

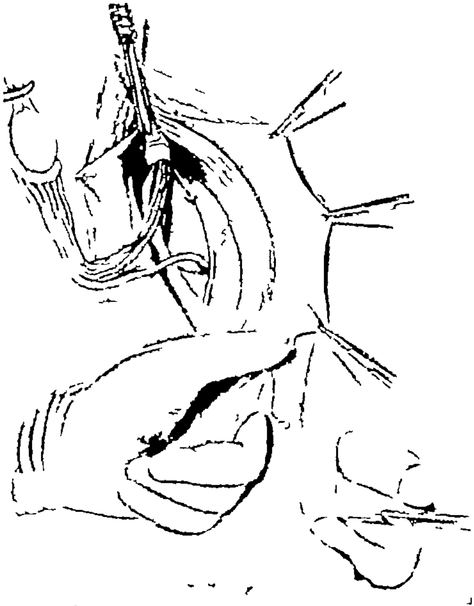

FIG 2 Index finger is then passed into scrotum and a separate transverse incision is made in scrotum 1 cm above bottom of scrotum This is not deepened beyond subcutaneous layer

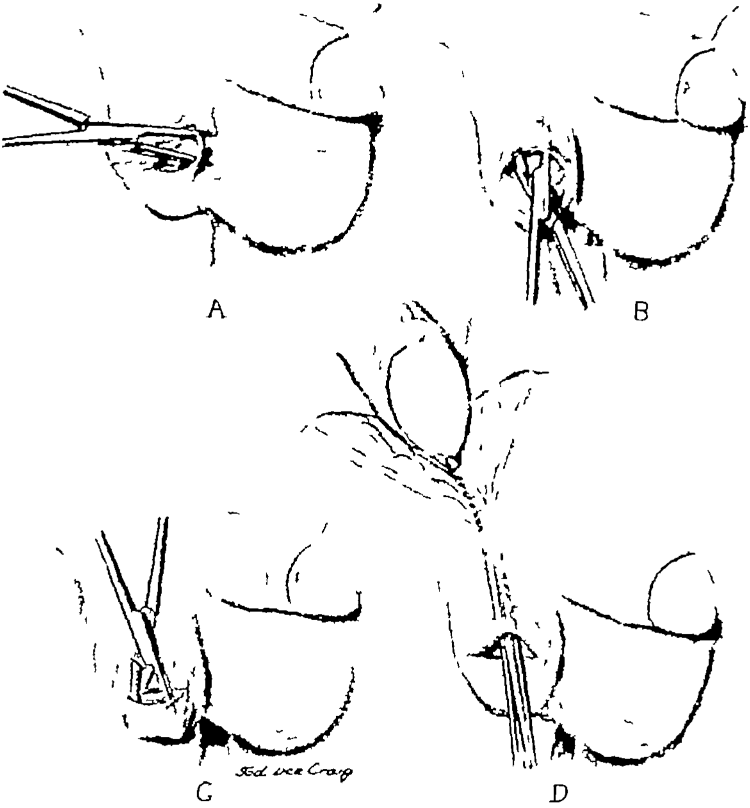

FIG 3 A subcutaneous superficial pouch is made, just beneath skin, but outside dartos, with a sharp pointed mosquito clamp This pouch should be made slightly larger than testis and its tunics A hole is made in dartos and testis is pulled down into scrotal pouch

tions about the incision for a sufficient distance in order to be absolutely sure that the subcutaneous scrotal pouch will be large enough to accommodate the testis and its membranes The finger can be inserted down into the scrotum from the inguinal incision and the scrotal incision made over the finger tip It is our practice to close the scrotal incision with interrupted sutures of 00000 atraumatic chromic catgut which does not necessarily have to be removed if the patient is especially fearful The sutures will eventually soften and come out as the child takes his tub baths, but may be removed if they persist unusually long

As in any other type of orchiopexy, it is essential to liberate the spermatic

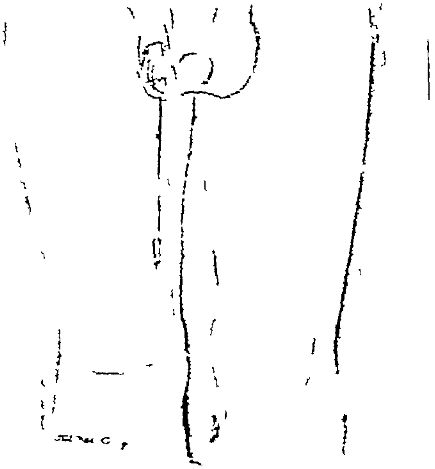

FIG 4 A traction suture of medium silk is passed through lower pole of testis and out through skin at most dependent point on scrotum Very gentle traction is maintained on silk suture by a rubber band, under mild tension, which is taped to knee for ten days Silk traction suture must not be brought out through skin incision during ensuing days

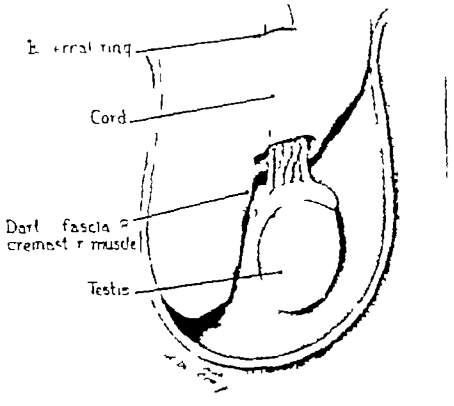

FIG 5 Schematic representation of subcutaneous scrotal pouch between skin and dartos Testis thus lies outside all muscular layers of scrotum and there is less chance of its being pulled upward by contraction of scrotal musculature Results with this technique during past 10 year period have been good

vessels beyond their junction with the hernial sac and the ductus deferens Strands of fascia which accompany the ductus deferens and the spermatic vessels can be cut and additional length of the cord will be gained thereby If insufficient length of vessels is obtained through the ordinary inguinal incision, the incision can be extended upward and the conjoined tendon incised so as to expose the spermatic vessels up to their origins from the aorta and vena cava. If they are dissected high enough, they will stretch sufficiently to permit the testis to reach into the scrotum. Likewise, it may be necessary to dissect the ductus deferens well down into the pelvis in order to achieve maximum length. While it is rarely necessary to pass the spermatic vessels and ductus deferens under the inferior epigastric vessels, this can be done if the surgeon is compelled to make an extraordinary effort to gain all the length possible. It is our feeling that this maneuver adds very little additional distance, but we do use it in cases where the cord is very short.

In making the closure it is our practice to close the transversalis fascia above the spermatic cord and to pull the conjoined tendon over to the shelving edge of Poupart's ligament with several interrupted sutures of chromic catgut, also above the cord. The fascia of the external oblique is closed with interrupted sutures of chromic catgut and the subcutaneous fat is closed with interrupted sutures of plain catgut. In small children it is important to close the superficial subcutaneous fascia and the subcutaneous fat carefully with many sutures lest the suture line spread and become unsightly. The skin is closed with interrupted sutures of fine silk. It is our practice to keep these children on strict bed rest 10 days following operation and to inspect the traction on the elastic band at least daily. Otherwise the traction will become too loose and the testis will recede towards the external ring. Excessive edema may occur if the traction is too strong.

After the child leaves the hospital it is important that the mother or father be carefully instructed to pull downward on the operated testis for ten long and forceful pulls each morning and night. If the child is large enough he can be taught to do this. One must be on guard against the parent or patient who will not perform the maneuver correctly, since many families will be content merely to pull on the skin of the scrotum without actually getting a good grip on the testis. If traction can be applied to the testis by this method twice daily for a period of six months after the operation, the cord will grow longer and more flexible with each succeeding month. If no such traction is applied, the cord will remain only as long as it was at the time of operation. It is recognized that there is some psychological hazard in advising this maneuver, but this is a calculated risk which must be taken in the interest of ensuring a satisfactory technical result.

SUMMARY

A technique which places the operated testis outside the dartos and cremaster, in a subcutaneous pouch in the scrotum, has been described. In this position there is less chance that the contractions of the dartos and cremaster will cause retraction of the testis during the postoperative period. The parents are advised to exert traction on the testis twice daily during the first six months postoperatively in order to ensure proper length on the cord.

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A STUDY OF IRRIGATING MEDIUM EXTRAVASATION DURING TRANSURETHRAL SURGERY

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During 1955 two patients at Temple University Medical Center in whom severe abdominal pain and rigidity developed during transurethral resection were studied by postoperative cystography This revealed two extravasations (fig 1) which required suprapubic drainage and repair Previously we had noted, during transurethral resection, the occasional occurrence of transient abdominal pain which subsided postoperatively, we thought that it might be due to extravasation

These two factors prompted the following postoperative study of two hundred consecutive cases of transurethral resection for evidence of extravasation as demonstrated by 1) cystography and 2) vascular hemolysis, using two irrigating media In the first hundred cases, distilled water was used, in the second hundred 1 1 per cent glycine was the medium

REVIEW OF THE LITERATURE

A Extravasation No reports have been made on the incidence of extravasation The only ones published concern cystography when rupture is suspected Kenyon stated, "If it were feasible to perform urethrocystography at the end of every transurethral prostatectomy, I believe the number of unsuspected perforations that occur and that heal with catheter drainage alone would be surprising " Goodwin and associates are of the opinion that minor perforations should be dealt with by watchful waiting The incidence of rupture following transurethral surgery has been reported many times in percentages ranging from 1 5 per cent to 2 8 per cent (King and Werner, Nesbit, Polse) Polse who summarized more than two thousand cases found 52 ruptured bladders with 12 deaths (2 3 per cent extravasated, 0 5 per cent mortality) Several authors have commented on the severe local effects of the extravasated medium (Ebert and Bavetta, McLaughlin, Bowler and Holyoke) McLaughlin and associates felt that some nephrotoxic substance may be released from the fat and muscle following extravasation of water Creevy commented that using 4 per cent glucose, he has frequently seen extravasation of irrigating fluid large enough to elevate the whole floor of the bladder cause no trouble " King and Werner reviewed a series of 10 cases of lower nephron nephrosis, and in every instance perforations of the prostatic capsule were described at operation

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Acknowledgement is made to the Mallinckrodt Chemical Works of St Louis which donated the urokon used in these cystograms

Acknowledgement is made to Dr W Edward Chamberlain, professor of radiology Temple University Medical Center whose department made the cystographic studies without charge

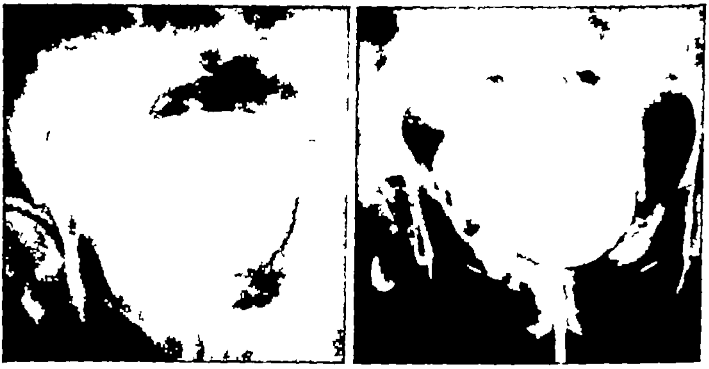

FIG 1 Postoperative cystograms taken in two patients with frank rupture of bladder that occurred during transurethral resection, suprapubic and extravesical drainage

B Hemolysis Creevy recently published an extensive review of the entire subject of hemolysis during transurethral surgery Foley first stated that he saw red ureteral efflux during a transurethral resection Emmett credited McLaughlin for first theorizing that irrigating fluid may enter the circulation Creevy stated that those who did complete transurethral prostatectomies saw postoperative renal failure not explicable by pyelonephritis, hemorrhage, shock, reactions to transfusions, nephrotoxic agents, or ureteral obstruction Harrison and associates, although agreeing with this concept, felt that hemolysis alone was not the sole factor for this failure Experimentally it has been shown that extremely high levels of free hemoglobin are required before renal damage occurs (Gilligan, Altschule and Katersky, Victor) It is doubtful if these levels are ever reached during resections Possibly hemoglobinemia causes constriction of intrarenal vessels and additional factors act in conjunction to produce subsequent renal damage

C Fluid absorption and electrolyte change Considerable evidence has accumulated to support Landes' suggestion to Goodwin and associates that severe hypertension during transurethral surgery may be due to the sudden large increase in the blood volume caused by the entrance of irrigating fluid into the vascular system (1951) A number of authors (Creevy, 1948, Jessop and Love, Landsteiner and Finch, Bulkley, O'Conor and Sokol, Hagstrom) have demonstrated that fluid absorption occurs Methods used by these workers in that demonstration include 1) Creevy (1948) showed that serum hemoglobin levels after resection averaged fifteen times the preoperative levels 2) Jessup and Love found postoperative hyperglycemia if glucose was used as the irrigating medium which was proportionate to the irrigating pressure 3) Landsteiner and Finch tagged irrigating solutions with salicylic acid and found, by postoperative levels, that an average of one liter of fluid was absorbed 4) Bulkley and associates demonstrated that a negative postoperative fluid balance occurred 5) Hagstrom used weight gain as a criterion and correlated it with resection time By these methods an average intake of 1000 cc and as much as 4000 cc during a prolonged resection was demonstrated Hagstrom reported a case of severe hypertension followed by shock, oliguria and uremia after transurethral resection and suggested that it was due to the hyponatremic syndrome. He credited Moyer with first making this suggestion.

Harrison and associates attributed the reaction manifested by severe hypertension, followed by shock and uremia, to fluid absorption in the aged or chronically ill, in whom even a minor change in the extracellular fluid and electrolyte pattern could precipitate the syndrome. They felt that dilutional hyponatremia followed the infusion of electrolyte-poor fluid, and that this sudden increase in blood volume could precipitate water intoxication. This in turn caused an increase in the cerebral blood volume followed by cerebral edema, resulting in an increase in the intracranial pressure with symptoms of elevation of blood pressure, slow pulse, nausea, vomiting, convulsions and coma. Pulmonary interstitial edema resulted in cyanosis. The duration of the cerebral signs was felt to be dependent on the time for redistribution, at which time dilutional hyponatremia became manifest.

In contrast, two limited studies (Murphy, Iob and Lapides; Nicolai and Cordonnier) reported no serum electrolyte change during transurethral surgery. Creevy (1948) stated that he had personally observed an example of acute hypochloremia with shock and felt that this concept should be more thoroughly investigated.

METHOD OF STUDY

The following procedures were carried out on 200 consecutive patients.

A. Cystography. All patients subjected to transurethral prostatectomy at Temple University Medical Center were studied immediately following their departure from the operating room. Cystography with 15 per cent urokon sodium was performed, filling the bladder through a Foley catheter, which was then pushed upward into the dome of the bladder to allow the prostatic bed to fill. One film was taken. The bladder was then emptied in order to reveal any small extravasation which would have been concealed by the intravesical contrast medium and another film exposed. Cystograms were read after the patients' discharge from the hospital in order not to affect the management of these cases and to preserve an unbiased opinion of extravasation not causing symptoms.

Cystograms were classified as follows (fig. 2):

1) No extravasation—no dye leaking from the fossa.

2) Minimal extravasation—definite projection of the contrast medium outside the capsule but limited to 0.5 cm. or less.

3) Moderate extravasation—definite projection outside the capsule farther than 0.5 cm.

4) Marked extravasation—definite collection of contrast medium outside of the capsule and some distance from it.

B. Serum analysis for hemolysis. Five cubic centimeters of blood were withdrawn from the antecubital vein into a clean dry syringe with a No. 20 gauge needle, allowed to stand, and then studied for hemolysis. According to Biorn and Greene, this is sufficiently accurate to detect significant hemolysis. The latter was classified by the color of the serum as follows:

1) Minimal—pink tinge.

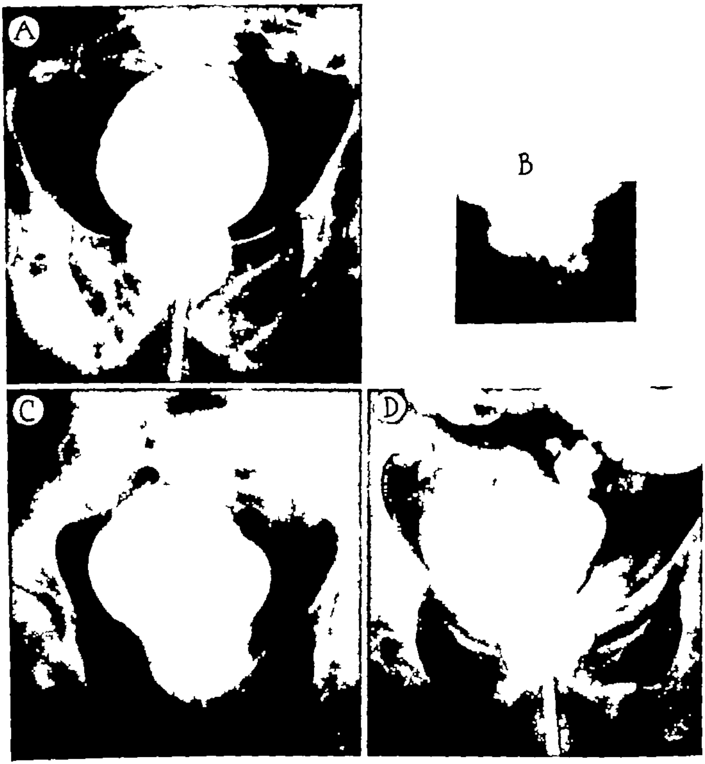

FIG 2 Postoperative cystograms illustrate degree of extravasation *A*, none, *B*, minimal *C*, moderate *D*, marked (See text for basis of classification)

2) Moderate—pink to light red
3) Marked—port wine to deep red

C Review of clinical course The anesthetic and postoperative records were carefully studied and analyzed

RESULTS OF STUDY

A series of 200 patients is presented, all of whom had postoperative cystograms and serum study for hemolysis Of these patients, 181 had benign prostatic hyperplasia and 19 had carcinoma of the prostate

A Incidence of extravasation and hemolysis Of the 200 cases studied, 48 (24 per cent) showed varying degrees of extravasation of the contrast medium (table 1) Twenty were classified as minimal, 14 as moderate, and 14 as marked extravasation

Table 2 reveals that 47 (47 per cent) of the first 100 patients on whom water was used as the irrigating medium showed varying degrees of hemolysis (18 showed minimal, 15 moderate, and 14 marked hemolysis) In the second 100 cases when 1 1 per cent glycine was used hemolysis was eliminated entirely

In tables 3 and 4 an attempt has been made to correlate hemolysis with extravasation as these occurred in the first 100 cases In the minimal extravasated group (13 cases) the incidence of hemolysis was 45 per cent Of the moderately

TABLE 1 *Incidence of extravasation as demonstrated by postoperative cystography*

Type of Irrigating Fluid	Number of Cases	Minimal Extravasation	Moderate Extravasation	Marked Extravasation	Total
Water	100	13	3	2	18
Glycine	100	7	11	12	30
Total	200	20	14	14	48
Percentage		10	7	7	24

TABLE 2 *Incidence of postoperative hemolysis*

Type of Irrigating Fluid	Number of Cases	Hemolysis			
		Minimal	Moderate	Marked	Total
Water	100	18	15	14	47
Glycine	100	0	0	0	0

TABLE 3 *Incidence of hemolysis (water series) in patients with demonstrable extravasation*

Degree of Extravasation	Number of Cases	Hemolysis		Percentage
		No	Degree	
Minimal	13	6	minimal 1 moderate 2 marked 3	45
Moderate	3	3	marked 3	100
Marked	2	2	moderate 1 marked 1	100
Total	18	11		61

extravasated group (three cases) and the markedly extravasated group (two cases) all (100 per cent) revealed hemolysis on postoperative serum study

Conversely in the minimal hemolysis group of 18 cases, only one showed extravasation, and that was minimal (table 4) Of the 15 cases of moderate hemolysis three (20 per cent) showed extravasation Finally, in the markedly hemolyzed group (14 cases) seven extravasations occurred (50 per cent) This demonstrates that hemolysis is a more sensitive index of fluid absorption from the prostate than is cystography in cases in which distilled water is used as the irrigating medium

Demonstration of direct venous filling with dye In three cases in this series a direct filling of the venous drainage of the prostate was shown The *iliac* vein and inferior vena cava were outlined in two cases (fig 3)

Reflux Reflux up one or both ureters was an incidental finding in 12 cases (6 per cent) (fig 4)

B Clinical effect of fluid exchange through the prostatic capsule It will be noted from the foregoing figures that the 200 patients have been classified into various

TABLE 4 *Hemolysis occurring without demonstrable extravasation*

Degree of Hemolysis	Number of Cases	Extravasation		Percentage
		No Cases	Degree	
Minimal	18	1	minimal 1	5 5
Moderate	15	3	minimal 2 marked 1	20
Marked	14	7	minimal 3 moderate 3 marked 1	50
Total	47	11		23

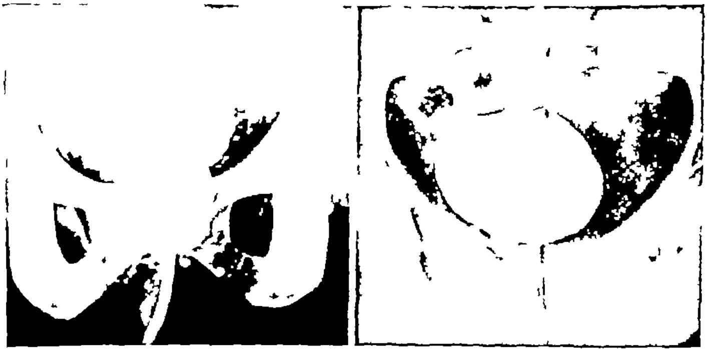

FIG 3 Postoperative cystograms show direct filling of venous drainage of prostate

groups depending on the degree of extravasation or hemolysis Since the purpose of this study was to observe the clinical effect, if any, of these factors, it was thought simpler to divide all patients into two major groups depending on the degree of fluid absorption from the prostatic bed The classification follows (table 5)

1) Low absorption group This includes all patients in the water and glycine series presenting little or no evidence of absorption of the irrigating medium in significant amounts as evidenced by a) negative extravasation in both groups and b) negative or minimal hemolysis in the water group The water series contained 64 cases of low absorption and 70 cases in the glycine series

2) High absorption group This includes all patients in whom significant amounts of fluid absorption were presumed to have occurred as evidenced by a) extravasation of any degree in the water and glycine series and b) moderate or marked hemolysis in the water series Thirty-six cases belonged in the group resected with water, and 30 in the glycine series (table 5)

Table 6 presents in detail the comparison and incidence of morbidity and mortality in the high and low absorption groups as they occurred in significant factors in both the water and glycine series They were compared in the following points

1) Hypertensive syndrome In 11 patients in the entire series, all in the high

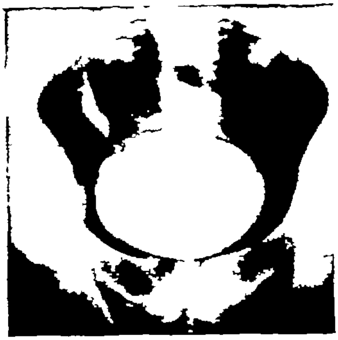

Fig 4 Postoperative cystogram demonstrates right ureteral reflux

Table 5 *Low and high absorption groups and distribution in water and glycine series*

Irrigating Medium	Number of Cases	Low Absorption Group	High Absorption Group
Water	100	64	36
Glycine	100	70	30
Total	200	134 (67%)	66 (33%)

Table 6 *Comparison of morbidity and mortality in high and low absorption groups*

Type of Complication	Number of Cases	Number and Percentage of Cases Occurring in High Absorption Group (66 Cases)			Number and Percentage of Cases Occurring in Low Absorption Group (134 Cases)		
		Water	Glycine	Total	Water	Glycine	Total
Hypertension syndrome	11	5 7%	6 9%	11 16%			
Postoperative hypotension	10	4 6%	5 7%	9 13%		1 0 7%	1 0 7%
Oliguria-uremia syndrome	5	4 6%	1 1 5%	5 7 5%			
Mortality	3	2 3%		2 3%	1 0 7%		1 0 7%

absorption group (five in the water group and six in the glycine group) a syndrome developed during the resection that was manifested by a marked rise in blood pressure after 30 to 60 minutes of the procedure This was usually accompanied by nausea and vomiting apprehension restlessness and in two cases cyanosis convulsions and coma The pulse rate was not correspondingly increased The rise in systolic blood pressure was between 70 and 90 mm mercury On cessation of the resection the blood pressure returned to preoperative levels

The prognostic significance of the hypertensive syndrome is illustrated in table 7 Eight cases (72 per cent) of the eleven acquired postoperative hypotension subsequently in four (36 per cent) the oliguria-uremia syndrome developed and death occurred in two (18 per cent) All of these hypertensive patients in the water group had moderate or marked hemolysis Nine patients had extravasation of various degrees All eleven of the patients could be classified preoperatively in the poor risk category because of cardiovascular disease malnutrition and other disease

2) Postoperative hypotension (table 6) Ten cases of postoperative hypo-

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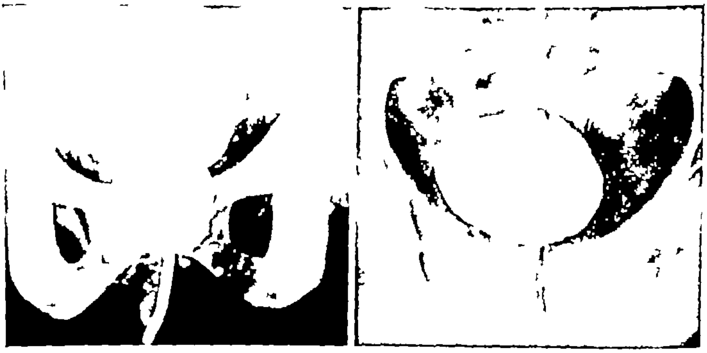

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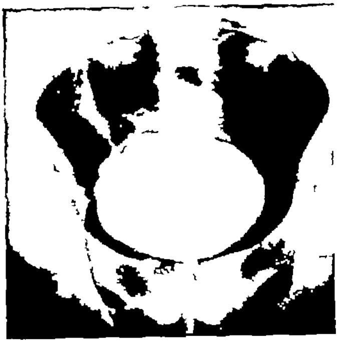

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TABLE 7 *Incidence of morbidity and mortality in patients with hypertension syndrome*

Type of Complication	Number of Cases	Number and Percentage of Cases Occurring in Group with Operative Hypertension (11 Cases)		Number and Percentage of Cases Occurring in Group without Operative Hypertension (189 Cases)	
Postoperative hypotension	10	8	72%	2	1%
Oliguria uremia syndrome	5	4	36%	1	0 5%
Mortality	3	2	18%	1	0 5%

tension developed in the entire series, nine were in the high absorption group and one in the low absorption group Postoperative hypotension was defined as a fall in systolic blood pressure from the average preoperative and operative levels to a reading at least 50 mm mercury below the average readings and to a point always below 90 mm mercury systolic despite adequate blood replacement This hypotension lasted from 30 minutes to several hours before correction As stated previously, eight of the 10 cases of hypotension fell into the group that had hypertension in the operating room The remaining two cases did not follow operative hypertension

3) Oliguria-uremia syndrome Five cases of the syndrome occurred in the entire series, all in the high absorption group (four in the water series and one in the glycine group) Oliguria was defined as a postoperative output of less than 300 cc on any postoperative day Uremia was defined as a blood urea nitrogen rise from normal to more than 30 (All five cases went above 100)

Four of the five cases presented the hypertensive syndrome in the operating room All of these cases had postoperative hypotension Two deaths occurred in this group The other three recovered after a prolonged hospital stay and were discharged in good condition without uremia All cases in the water group had marked hemolysis Four of the five cases had extravasation on cystography

4) Mortality Three deaths occurred in the entire series, all in the water group, an over-all mortality rate of 1 5 per cent Two occurred in the high absorption group and one in the low absorption group In both cases in the high absorption group the hypertensive syndrome developed in the operating room, followed by hypotension and the oliguria-uremia syndrome Of these, one died, after the diuretic phase was over, of a pulmonary embolus 16 days postoperatively The other died of a coronary occlusion six days following surgery The one death in the low absorption group was due to massive pulmonary embolus 12 days post-prostatectomy and five days post-transurethral hemostasis

5) Other factors In reviewing various factors that produced high absorption, the only two found to have a direct bearing on this occurrence were a combination of a prolonged operating time with visible capsular nicks A prolonged procedure was classified as one lasting more than 60 minutes from the time the resection was started Fifty-eight cases in the entire series were more than 60 minutes in length Definite capsular nicks with a Swiss cheese appearance of the wall of the fossa, described by the surgeon at the time of the resection, were noted 53 times The combination of nicks associated with a lengthy procedure occurred 20 times In this combination 16 patients fell in the high absorption

TABLE 8. *Incidence of high absorption in patients undergoing transurethral resection that lasted more than 60 minutes, and in whom capsular nicks were seen*

Factor	Number of Cases	Number and Percentage of Cases Occurring in High Absorption Group (66 Cases)		Number and Percentage of Cases Occurring in Low Absorption Group (134 Cases)	
Capsular nick seen with procedure over 60 minutes	20	16	24%	4	3%

group (table 8). Thus the combination indicates a much higher probability of fluid absorption of a significant degree. Capsular nicks or increased length of procedure alone do not appear to have any correlation.

Other factors such as abdominal pain, age, nature of pathologic lesion, weight of tissue and blood transfusion in the operating room did not appear to vary significantly between the high and low absorption groups.

Transient abdominal pain was frequently absent despite marked extravasation on cystography and meant visible extravasation only 50 per cent of the time (15 cases of pain, seven of which showed no extravasation on cystography).

DISCUSSION AND CONCLUSIONS

Extravasation and fluid absorption. Transurethral prostatectomy is frequently accompanied by extravasation from the prostatic bed, as demonstrated by postoperative cystograms in 200 consecutive cases. In these patients, definite extravasation of the contrast medium was seen in 48 cases (24 per cent). That absorption can occur directly into the veins is further evidenced by the fact that an outline of the pelvic venous system was seen in three cases during postoperative cystography.

The aforementioned fact, together with the high incidence of serum hemolysis (47 per cent) in cases in which distilled water was used as an irrigating medium, should serve to re-emphasize that fluid absorption from the prostatic bed occurs in transurethral prostatectomy.

This series of 200 cases demonstrates that the incidence of morbidity and mortality is significantly higher in patients absorbing large amounts of fluid during the procedure.

Management of extravasation and fluid absorption. A) Extravasation. Radiographic evidence of extravasation by itself is not sufficient to indicate postoperative surgical intervention. In the group of 48 cases, none required repair or acquired pelvic cellulitis. It is only when frank evidence of rupture occurs, with a discrepancy in the measured amount of fluid going in and out of the bladder, accompanied by abdominal pain and rigidity, and cystographic evidence of a sizable fluid collection that repair is necessary.

B) Prevention of excessive fluid absorption. The amount of absorption increases as the larger venous channels near the capsule are exposed, and significant venous bleeding follows. This type of bleeding is easily recognized as it is profuse when the bladder is empty or partly filled and stops when the bladder nears its capacity and rising intravesical and intraprostatic pressure exceeds the

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venous pressure At this point this intravenous infusion can be limited by observing the following principles, suggested in part by a number of investigators (Griffin, Harrison, Boren and Robison, Nesbit, 1943)

1) The capsule should not be exposed until the conclusion of the operation This will prevent prolonged absorption of fluid

2) The time of the procedure should be limited after capsular nicks or excessive venous bleeding is demonstrated

3) Attempts to stop venous bleeding by fulguration are fruitless and potentially dangerous, as the beak of the resectoscope sheath is aimed directly at the vein and may stretch the capsule and allow more rapid absorption

4) The water level should be kept as low as feasible, and should never be raised to aid vision when venous bleeding occurs

5) Intravenous fluids are unnecessary and should only be given slowly as a means of keeping the needle open for blood replacement

6) The development of hypertension during the procedure means that an excessive amount of fluid has entered the circulation Its appearance should be followed by quick hemostasis, discontinuance of the operation, and administration of hypertonic saline intravenously

7) The goal of complete capsular exposure is unwise in view of increased fluid absorption Instead, one should aim at almost exposing the capsule, and leaving a smooth concavity in the prostatic fossa This can be achieved by partly exposing the capsule in one or two quadrants as a guide to the depth of resection

8) Although the use of isotonic fluids does not prevent excessive fluid absorption, there is no doubt that hemolysis associated with excessive absorption of water increases the incidence of oliguria and uremia For this reason, isotonic fluids, such as 1 1 per cent glycine, should be used as the irrigating medium

Attention to the foregoing principles will further minimize the hazards of an already proven and safe operative procedure

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rhagic disorder It is suggested by some hematologists that a family tree be plotted through the grandparents for each patient Certainly much attention should be given to the patient's description of prolonged epistaxis, gastrointestinal bleeding, particularly hemarthroses, unexplained hematuria, and ecchymoses in soft tissue which seem out of proportion to the trauma which preceded them Initial laboratory tests on all patients suspected of bleeding disorders should include a platelet count, bleeding time, a tourniquet test, and a whole blood coagulation time MacFarlane and Biggs divide the patients into two groups 1) those with an abnormal one-stage prothrombin time, and 2) those with a normal one-stage prothrombin time Hemophilia is included in the group with a normal one-stage prothrombin time When such a disorder is suspected, the services of a good hematology department are mandatory in the proper diagnosis and management of the patient

Successful major surgery has been performed many times on hemophiliacs Hinman reported a successful perineal prostatectomy on a hemophiliac in 1933 Mathé and Mitchell successfully performed fulguration of a prostatic median bar which they reported in 1929 A hemophiliac who survived a nephrectomy was reported by Vermooten in 1950 These appear to represent the only cases of successful major urologic surgery in hemophiliacs to date Craddock, Fenninger and Simmons reported a mortality of 27 per cent in their review of patients who underwent internal surgery up to 1948 An analysis of the cases in table 1 indicates that this figure might be conservative for patients in whom a positive laboratory diagnosis of hemophilia has been made Three out of seven such patients succumbed following major surgical procedures, a mortality of approximately 44 per cent There is reason to wonder about a diagnosis of hemophilia in some of the reported cases The case of a patient who is a proven hemophiliac and who had a total prostatectomy is presented

CASE REPORT

D A, University Hospital No 071-1-90, a 56-year-old school bus driver, was admitted March 2, 1955 with a complaint of urinary retention He was referred from Keyser, West Virginia where a catheter had been inserted and taped in place by Dr Robert T Coffman He was known to have a bleeding tendency The patient described large areas of discoloration which frequently followed slight trauma or strain He had several episodes of epistaxis requiring packing of his nose He bled for 10 days following an extraction of a tooth Until the age of twenty he frequently used crutches because of pain and swelling in his ankles and knees Since then he had had no difficulty in walking He had bouts of hematemesis and hemoptysis Nine years prior to this admission he noticed a decrease in the size and force of his stream Urinary retention developed one and one-half weeks prior to admission He gave no family history of hemorrhagic disorders His father died with arteriosclerosis at the age of eighty-four and his mother died at the age of sixty-four with a stroke Two of his children had diabetes described as being of a slight degree in that neither required insulin It is now known that one of his grandchildren has hemophilia

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PROSTATECTOMY IN A HEMOPHILIAC

JOHN D YOUNG, JR AND MILTON S SACKS

From the Divisions of Urology and Hematology, University of Maryland School of Medicine, Baltimore, Md

Tendencies toward excessive bleeding are of considerable interest to the urologist While the intricate physiology of blood clotting along with its many theories and controversies is beyond the scope of urology, it is fitting that we give some thought to this mechanism without which urologic surgery would be practically impossible

Hemophilia can best be defined to the surgeon as one of several hemorrhagic diatheses which contribute to alarming hemorrhages Hemophilia is defined by the hemotologist as that condition caused by a deficiency of a specific clotting factor known as the anti-hemophilic globulin This substance is concerned with the generation of thromboplastin Quick has therefore called the substance thromboplastinogen MacFarlane and Biggs outline a possible order of interaction of the factors concerned in blood clotting

1 Antihemophilic globulin + Platelets $\xrightarrow{\text{Christmas factor}}$ Intermediate product

2 Intermediate product + Factor V $\xrightarrow{\text{Factor VII}}$ Thromboplastin

3 Prothrombin $\xrightarrow{\text{Thromboplastin}}$ Thrombin

4 Fibrinogen $\xrightarrow{\text{Thrombin}}$ Fibrin

The deficiency of antihemophilic globulin as the cause of hemophilia is stressed because the term, hemophilia has been used loosely for other hemorrhagic disorders which should be managed quite differently

The etiology of the disease is not known The majority of hemophiliacs have inherited the defect as a sex-linked recessive characteristic MacFarlane and Biggs report more recently that as high as twenty-five per cent of patients with this disease cannot trace it from any ancestor in the family tree It is stated further that the presence of this hemorrhagic disorder in infancy almost always indicates heredity as the cause while its appearance in later life is less apt to be attributed to inheritance It was formerly thought that hemophilia had clinical manifestations in only males while females acted as carriers Brinkhous produced hemophilia in the female dog by mating an affected male with a carrier Spaet in his excellent review of this subject stated that such a mating in the human would be apt to occur in one in one hundred million marriages Female patients with hemophilia have been reported by Israels and others, and Merskey

The history is of major importance in the diagnosis of hemophilia A patient who has bled for more than twenty-four hours following a minor surgical procedure such as a tooth extraction should be suspected of having such a hemor-

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Read at annual meeting of Mid Atlantic Section, American Urological Association, Virginia Beach, Va , March 21-23, 1957 minutes, 33 minutes, and 42 minutes The thromboplastin generation test showed an abnormality of the antihemophilic globulin An assay showed a deficiency of the antihemophilic globulin An intravenous pyelogram showed no obstruction of the upper urinary tract The cystogram showed prostatic enlargement He had periodic gross hematuria through his catheter

The hematologist thought a prostatectomy might be possible if the patient were to receive fresh blood or plasma at eight-hour intervals preceding and following the procedure The only alternative appeared to be tube drainage of some type which was also fraught with the dangers of urinary tract bleeding

On March 26 a total perineal prostatectomy was performed under saddle block anesthesia This procedure was elected so as to leave no bleeding fossa All bleeding vessels were ligated as meticulously as possible The bladder neck was anastomosed to the membranous urethra A Penrose drain was left in place The patient was given 200 cc fresh plasma or fresh whole blood at 8-hour intervals Whole blood was used in amounts required to replace loss Plasma was used when replacement was not required The patient bled from his wound and a large hematoma formed between the rectum and pubic arch It was somewhat advantageous that the bleeding was confined to this area The bleeding probably would not have been so well confined had the incision been made in the lower abdomen The hematoma caused some rectal obstruction On the fifth postoperative day Wangensteen suction was instituted through a Levine tube in the stomach The hematoma was drained by separating one side of the wound on the eighth postoperative day The postoperative hemoglobin reached its lowest point on the ninth postoperative day of 6 8 gm He had his first bowel movement on the eleventh postoperative day The perineal wound separated as a result of the hematoma Severe hematuria with clot retention for the first time developed on the seventeenth postoperative day At this time he began passing urine through the perineal incision He was again placed on fresh plasma or blood every eight hours The bladder was allowed to remain distended as a form of tamponade against the bleeding His blood urea nitrogen reached its highest point of 39 mg per cent at this time The tip of the catheter was found to be protruding through the perineal incision on the twenty-fourth postoperative day A filiform and a No 12 Philips catheter was passed easily into the bladder on the thirty-first postoperative day He continued to bleed periodically from the bladder and from the granulating perineal wound Acute epididymitis developed on the twenty-ninth postoperative day He had no significant bleeding after the thirty-third postoperative day Streptomycin, penicillin, gantrisin, terramycin and mandelamine had been used to combat infection during his postoperative course After having received 34 pints of fresh blood and 13½ pints of fresh plasma the patient was discharged from the hospital on catheter drainage on his sixty-eighth postoperative day After removal of the catheter, approximately one month after discharge, the patient voided well with good sphincter control He occasionally leaked some urine through the perineal fistula

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TABLE 1—*Reported cases of major "internal" surgery in hemophilia**

Associated Disease and Authors	Operation	Outcome	Criteria of Diagnosis of Hemophilia				
			Lab data	Family history	Past history	Sex	Positive diagnosis
Bladder polyp prostatic median bar (Mathé and Mitchell)	Polypectomy Fulguration of median bar	Recovery	–	–	±	M	
Prostatic hypertrophy (Hinman)	Perineal prostatectomy	Recovery	–	±	+	M	
Hydronephrosis with infection (Mertz Meiks)	Nephrectomy	Death	+	±	+	M	Yes
Peptic ulcer with hemorrhage (Wosnessensky)	Gastric resection	Death	0	0	0	M	
Peptic ulcer with hemorrhage (Emile and Weil)	Gastroenterostomy	Recovery	+	±	+	M	Yes
Appendicitis (Emile and Weil)	Appendectomy	Recovery	+	0	0	0	
Tonsillitis and appendicitis (Hays)	Tonsillectomy Adenoidectomy Appendectomy	Recovery	–	0	0	M	
Appendicitis (Vance)	Appendectomy	Death	±	0	0	M	
Appendicitis (Birch)	Appendectomy	Death†	+	+	+	M	Yes
Appendicitis (Prima)	Appendectomy	Recovery	0	0	0	M	
Appendicitis (Cioran)	Appendectomy	Recovery	+	+	–	M	Yes
Appendicitis (Hipsley)	Appendectomy	Recovery	0	±	+	M	
Appendicitis (Paz)	Appendectomy	Recovery	0	–	+	M	
Ruptured spleen (Friedrich)	Splenectomy	Recovery	0	+	0	M	
Gastrointestinal bleeding (Friedrich)	Gastric resection	Recovery	0	+	+	M	
Appendicitis (Craddock Fenninger Simmons)	Appendectomy	Death	+	+	+	M	Yes
Calculus pyonephrosis (Vermooten)	Nephrectomy	Recovery	+	U	+	M	Yes
Prostatic hypertrophy (present report)	Total perineal prostatectomy	Recovery	+	–	+	M	Yes

* Table from Craddock Fenninger and Simmons with 2 added cases of Vermooten and this report

† Patient survived operation one week but died with postoperative hemorrhagic pneumonia

Symbols + Positive findings – Negative findings ± Questionable or inadequate findings 0 data not given U Unknown (adopted child)

Physical examination showed a well developed man in no apparent distress The blood pressure was 142/80, pulse rate was 76 A large ecchymotic area was present in the lateral portion of the right upper arm A swollen nodule was lateral to the left deltoid region No joint deformity was present other than a flexion contracture of the left little finger The lung fields were clear, the heart was not enlarged and the rhythm was regular No abdominal masses were felt A retention catheter was in place The prostate was about three times normal size without any palpable evidence of malignancy The admission hemogram showed hemoglobin 15 0 gm (109 per cent), erythrocytes 5,620,000, hematocrit 50, platelet count 996,800, reticulocyte count 0 4 per cent, prothrombin time 16 seconds or 50 per cent of normal, leukocytes 15,700, with 85 segmented and 1 non-segmented cell, 12 lymphocytes and 1 eosinophil Admission blood chemistries showed sugar 67 mg per cent, urea nitrogen 18 mg per cent, carbon dioxide 60 meq/L, chlorides 110 meq/L, albumin 4 5 gm per cent, globulin 2 5 gm per cent, sodium 140 meq/L, potassium 5 7 meq/L, serologic test for syphilis negative The bleeding time was two and one-half minutes The clot retraction test was normal Serum was expressed within two hours His blood type was O Rh negative The capillary fragility test was negative The coagulation time was 18 minutes, 33 minutes, and 42 minutes The thromboplastin generation test showed an abnormality of the antihemophilic globulin An assay showed a deficiency of the antihemophilic globulin An intravenous pyelogram showed no obstruction of the upper urinary tract The cystogram showed prostatic enlargement He had periodic gross hematuria through his catheter

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DISCUSSION OF THERAPY

MacFarlane and Biggs warn that "the mortality in major operations, even with massive transfusion therapy, is very high " It becomes readily apparent that major surgery should be undertaken only with great caution in the presence of hemophilia The only known effective means of reducing the coagulation time in vivo in a hemophiliac is by the transfusion of fresh blood or plasma or a preparation of the globulin fraction of plasma containing the antihemophilic factor This factor may be present in stored blood from a few hours to several days The antihemophilic factor is retained for many months in plasma which has been dried or frozen soon after its withdrawal While transfusions with as little as 50 cc plasma might reduce the coagulation time of the blood of a hemophilic patient to within normal limits for as long as twenty-four hours, this does not assure the hemostatic efficiency of the clotting mechanism A level of about thirty per cent of antihemophilic globulin must be obtained in the blood to produce a normal clotting mechanism The tendency is to give larger amounts of fresh whole blood or plasma rather than the frequent small amounts formerly used To reach a level of 30 per cent of antihemophilic globulin in a rather severe hemophiliac, MacFarlane and Biggs estimate that the patient would have to receive a volume of fresh whole blood or plasma in an amount equal to half the total blood volume This is in effect one-half of a replacement transfusion with blood or plasma less than three hours of age Such a method of management has some possible advantage over the more frequent smaller transfusions used in the patient reported above Vermooten's patient was managed quite successfully with 44 units of antihemophilic globulin This substance has been quite expensive Some degree of resistance or tolerance has been noted to develop in hemophiliacs treated repeatedly with fresh transfusions or the antihemophilic globulin An antihemophiliac factor concentrate from bovine plasma has been prepared in MacFarlane's laboratories at Oxford It is stated that 1 gm of this product has the activity of 20 pints of normal plasma Three patients were given repeated doses of this substance while being subjected to dental extractions Spaet suggests the possibility that such an agent might some day be given like insulin for hemophilia

SUMMARY AND CONCLUSION

Hemophilia is a formidable hazard in major surgery There appears to be a mortality of about 40 per cent in hemophiliacs undergoing major internal surgery

A case is reported of a successful total prostatectomy in a hemophiliac The method of management includes the use of antihemophilic globulin, transfusion with fresh whole blood or fresh plasma and possibly a new antihemophilic factor concentrate from bovine plasma

University Hospital, Baltimore-1, Md

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UROLOGICAL COMPLICATIONS FOLLOWING USE OF RADIOACTIVE GOLD FOR CARCINOMA OF UTERINE CERVIX

M RICHARD CARLIN

From the Department of Surgery (Urology), Washington University School of Medicine St Louis, Mo

Recently, considerable controversy has developed over the management of carcinoma of the uterine cervix between the advocates of the surgical approach and the advocates of irradiation In general, it is agreed that both methods of therapy achieve approximately the same statistical cure rate in the League of Nations stage 1 and 2 lesions The reasons for failure by either method in these early cases can best be explained by the anatomical and pathological characteristics of this disease[1] Few patients are saved by operation when the regional lymph nodes are positive and similarly recurrences in irradiated patients are found frequently in the lateral parametrium These findings suggest that tumor cells are already outside the effective area of irradiation or operation at the time of initial treatment and markedly reduce the likelihood of cure If these assumptions are true, better results should be obtained by more effective methods of irradiating the lateral parametrium and the pelvic lymph nodes The parametrial injection of radioactive colloidal gold was introduced as a means of irradiating the parametrium with the hope that this method would increase the cure rates by treating the areas of lymphatic drainage This expectation has been realized as the over-all results have been better in cases treated with gold and radium than in cases treated with x-ray and radium[2, 3] However, in a small number of patients treated with radioactive gold, serious complications involving the genitourinary tract have occurred[4] For this reason, a review of the clinical aspects of these complications seems timely

All patients who were treated with radioactive gold were also treated by one or more of the conventional methods of therapy, that is, radium application and Wertheim hysterectomy The reasons for the variations in the therapeutic program have been explained in earlier publications by Allen and Sherman[5]

The preliminary experimental work on this subject has been published elsewhere[6-8] Radioactive gold was chosen for several reasons It has a short half-

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Read at annual meeting of American Urological Association Pittsburgh Pa May 6–9, 1957

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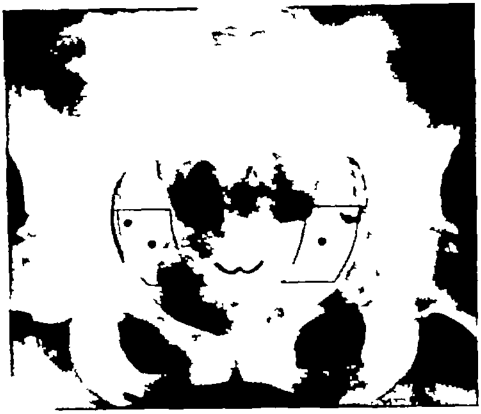

FIG 1 X ray taken immediately after injection of radioactive gold to which diodrast was added It demonstrates areas in pelvis which are subjected to irradiation by gold solution

life of 2 7 days and 90 per cent of its activity is in the form of beta particles This tends to give an excellent localizing radiation The gold is used in a colloidal suspension usually in a concentration of 1 5 to 2 mc per cc The technique of its use is quite simple With the patient in the lithotomy position the fornix to be injected is exposed and a No 22 gauge spinal needle is inserted into the paracervical area and carried through the mucosa, Mackenrodt's ligaments, and continued laterally, angled at 20 to 30 degrees from the midline, to approximate the pelvic wall As the needle is withdrawn the gold is injected Three sites of injection are selected in each parametrium giving a uniform dispersion of the gold throughout the area (fig 1)

MATERIAL

A total of 135 patients were treated by the injection of radioactive gold for carcinoma of the female genitalia at Barnes Hospital during the four-year period from January 1950 through December 1954 (table 1) Of these, 18 received an injection of radioactive gold followed by a Wertheim operation and pelvic lymphadenectomy Seventy patients received radioactive gold in combination with one or more implantations of radium In 42 patients the treatment consisted of radium implantation, radioactive gold injection, and a Wertheim operation One patient was treated with radioactive gold only, one with gold and external irradiation, and three with radioactive gold and pelvic evisceration

The pathological diagnosis was squamous cell carcinoma of the cervix in 126 patients (in four of these a supracervical hysterectomy had been done at an earlier date elsewhere), adenocarcinoma of the cervix in seven patients, and adenocarcinoma of the endometrium in two patients The patients ranged in age from 21 to 80 years at the time of initial treatment

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Sherman A I and Ter Pogossian M Lymph node concentration of radioactive gold following interstitial injection Cancer, 6 1238 1953

[5] Sherman A I Bonebrake M D Arneson A N and Ter Pogossian M Clinical results following different methods of radium application used in the treatment of cervical cancer Am J Roentgenol & Rad Ther 69 925 1952

TABLE 1 *Genitourinary complications following use of radioactive gold Total number of cases, 135*

Associated with primary disease		
Unilateral hydronephrosis	4	Recurrent tumor
Bilateral hydronephrosis	3	
Vesicovaginal fistula	2	
Vesicocutaneous fistula	1	
Renal tuberculosis		1
Incrusted cystitis		1
Not associated with tumor recurrence		
Irradiation cystitis		3
Periureteritis with hydronephrosis		4
Cystitis and hydronephrosis		3

The hospital charts of all of these patients were carefully reviewed In 113 cases no significant urological complaints or findings followed treatment The word, significant is used to emphasize the fact that many patients had symptoms and signs of mild or transient cystitis Thorough urological investigation was not done unless the symptoms were moderate or severe and persistent Some patients in this group may well have silent obstructive disease of the ureters which has not yet been discovered

In the remaining 22 patients, significant urological disease was demonstrated In 12 of these 22 the urological disease was associated with other clinical problems, usually recurrence or persistence of the tumor, and it was therefore impossible to evaluate the role of the radioactive gold as a causative agent In the group in which persistent tumor was subsequently demonstrated, four patients had unilateral hydronephrosis or nonvisualization by intravenous pyelography, three had bilateral hydronephrosis, two had vesicovaginal fistulas, and one had vesicocutaneous fistula An additional patient with unilateral hydronephrosis was proven to have renal tuberculosis by culture techniques, and tuberculous salpingitis was demonstrated in the specimen removed at the time of a Wertheim operation Another patient had severe alkaline incrusted cystitis which was thought to be related to a suprapubic cystotomy tube that had been inserted before coming to this hospital for treatment

The remaining 10 patients have had serious urological complications thought to be due to the treatment employed rather than to their original disease In general, these complications have fallen into three categories 1) irradiation cystitis alone (three cases), 2) irradiation periureteritis with hydronephrosis (four cases), 3) a combination of cystitis and periureteritis (three cases) Four representative cases will be reported

CASE REPORTS

Case 1 Irradiation cystitis B H No 240496, L G , a 57-year-old-white woman, was first hospitalized in July 1954 because of postmenopausal bleeding Initial examination revealed moderate hypertension and marked exogenous obesity A biopsy of the cervix was reported as squamous cell carcinoma, Broders' type 2 The clinical classification was League of Nations stage 2

On July 31, 1954, therapy was started with an intracavitary and intravaginal implantation of radium (4125 mg hours). In August 1954 60 mc radioactive colloidal gold was injected into each parametrium by the usual technique. For the week following this injection the patient complained of urgency, frequency, and dysuria. During the third hospitalization on August 28, 1954 she received the second implantation of radium (4125 mg hours).

The patient was admitted to the urology service in January 1955 with a history of gross total hematuria, the "passage of tissue in the urine," urgency, dysuria and marked frequency of two months' duration. An intravenous pyelogram was technically unsatisfactory because of the patient's obesity. Bilateral retrograde pyelograms were normal. Cystoscopy revealed a sharply demarcated ulcer, 4 cm in diameter, located on the right anterolateral wall of the bladder and covered by adherent calcific material. The trigone, ureteral orifices, and remainder of the bladder wall were normal. A transurethral biopsy of this lesion was performed with an attempt to resect all of the calcareous material. The surgical pathologist reported chronic cystitis with calcification, irradiation reaction. The patient's hematuria subsided after this treatment.

On her fifth admission in February 1955, the patient again complained of gross total hematuria associated with chills and fever. Bilateral costovertebral angle tenderness was the only significant physical finding. An intravenous pyelogram was negative. Cystoscopy revealed a lesion on the anterolateral wall of the bladder, as before. Again a transurethral resection of this ulcer was done and the pathology report was irradiation cystitis. This procedure controlled the hematuria and the patient was discharged.

The final hospitalization in March 1955 was precipitated by a recurrence of profuse hematuria three days before entry. The patient had a purpuric rash on the skin of the right thigh and three plus edema of the entire right lower extremity. The hemoglobin was 7 gm., the nonprotein nitrogen 22 mg. Bleeding, clotting and prothrombin times were normal. The patient was transfused immediately after admission, but the clinical picture of shock developed despite the administration of whole blood under pressure through both antecubital veins. Because of the uncontrollable bleeding, an emergency suprapubic cystostomy was done on the afternoon of admission.

The bladder was entered through a midline suprapubic incision. An area of necrosis of the bladder was found on the right anterolateral wall involving its entire thickness. No specific bleeding points could be identified and the bleeding could not be controlled by suture ligatures around the area of necrosis. The right half of the bladder was packed through the cystostomy incision and this seemed to control the hemorrhage. The postoperative period was complicated by fever and pulmonary consolidation, and the patient expired as a direct result of respiratory difficulties on the sixth postoperative day. Permission for an autopsy was not granted.

It is of interest that this patient's first urological complaints occurred immediately after the injection of radioactive gold and that the subsequent area of delayed radiation cystitis was located well away from the bladder base. The location of the lesion on the lateral bladder wall makes it unlikely that this was secondary to radium application Presumably, the radiation cystitis was secondary to a localized "hot spot" just outside of the lateral bladder wall due to a heavy local concentration of radioactive gold This was the only fatality in the entire series directly attributable to the use of gold

Case 2 Periureteritis with hydronephrosis B H No 48297, O B C, a 51-year-old Negro woman, was hospitalized because of postmenopausal bleeding *Cervical biopsy was reported as squamous cell carcinoma* The clinical classification was League of Nations stage 2 The remainder of the physical examination and basic laboratory tests were within normal limits

On May 5, 1953 radium was applied to the cervix in a colpostat (5250 mg hours) No immediate complications followed On May 23, 1953, 65 mc radioactive gold was injected into each parametrium in the usual manner On July 9, 1953 the patient returned to the hospital for the final radium application (1935 mg hours)

One month later the patient returned to the hospital because of nausea, vomiting, and lower abdominal pain The temperature and white blood count were moderately elevated The clinical diagnosis was pelvic cellulitis and good response followed administration of parenteral fluids and chemotherapy An intravenous pyelogram (fig 2, *A*) was interpreted by the radiology department as nonvisualization of the right kidney, hydronephrosis and hydroureter on the left, and a filling defect of the left half of the bladder

The patient's last hospitalization was in September 1953, at which time she again complained of nausea, vomiting, and lower abdominal pain The clinical

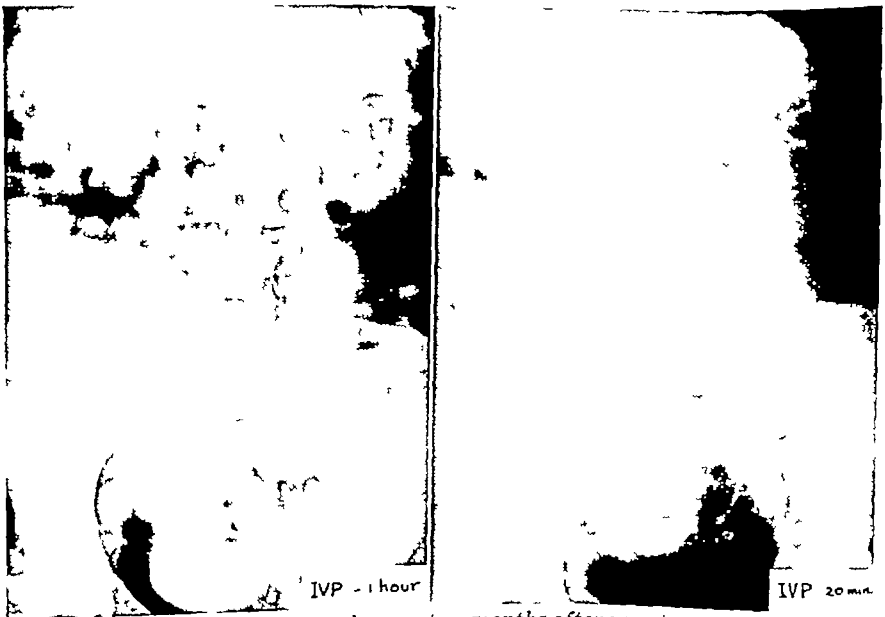

Fig 2 Case 2 *A*, intravenous pyelogram two months after injection of radioactive gold Note nonvisualization of right kidney in 60 minutes, hydronephrosis and hydroureter on the left *B*, intravenous pyelogram two and one half years after gold injection

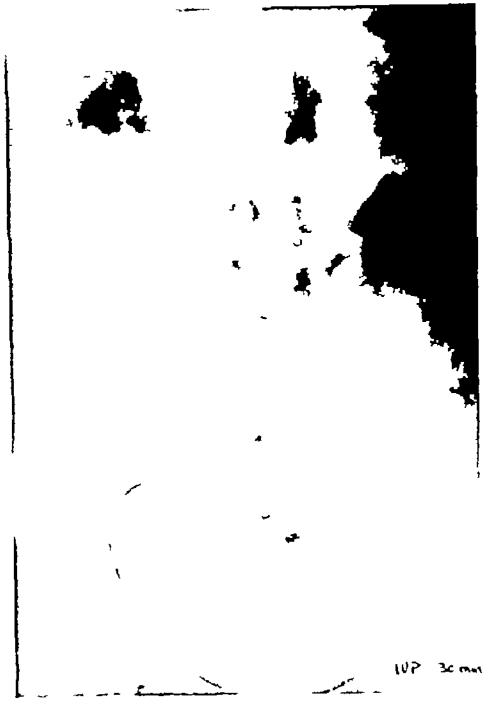

FIG 3 Case 3 Intravenous pyelogram one and one half years after gold injection demonstrates left ureteral obstruction just below pelvic brim

diagnosis was post-irradiation syndrome The nonprotein nitrogen was 17 mg per cent Improvement was noted after the administration of intravenous fluids and antibiotics Urological consultation was not requested

Following discharge, the patient was carefully followed in the Tumor Clinic She has remained free of symptoms and without evidence of recurrence Intravenous pyelograms were obtained in October 1956 (fig 2, *B*) because of the interest stimulated by this study The right kidney was not visualized at the end of two hours and the left collecting system was interpreted as normal

Since a complete urological study was never made in this case, it is difficult to draw any exact conclusions Nevertheless, the occurrence of bilateral ureteral obstruction is of interest The location of the point of obstruction on the left was just below the pelvic brim, that is, several centimeters above the usual site of ureteral injury due to radium The silent nature of the left hydronephrosis suggests extrinsic ureteral compression, the reversibility suggests radiation injury rather than metastatic tumor Certainly this case emphasizes the value of routine pretreatment pyelographic study

Case 3 Periureteritis with hydronephrosis B H No 234912, E A J , a 50-year-old-white female, was first examined because of postmenopausal bleeding A cervical biopsy was reported as squamous cell carcinoma The clinical evaluation was League of Nations stage 2 The patient had no past history of renal disease On April 18, 1954, radium was applied in a colpostat (3740 mg hours) On secondary to radium application Presumably, the radiation cystitis was secondary to a localized "hot spot" just outside of the lateral bladder wall due to a heavy local concentration of radioactive gold This was the only fatality in the entire series directly attributable to the use of gold

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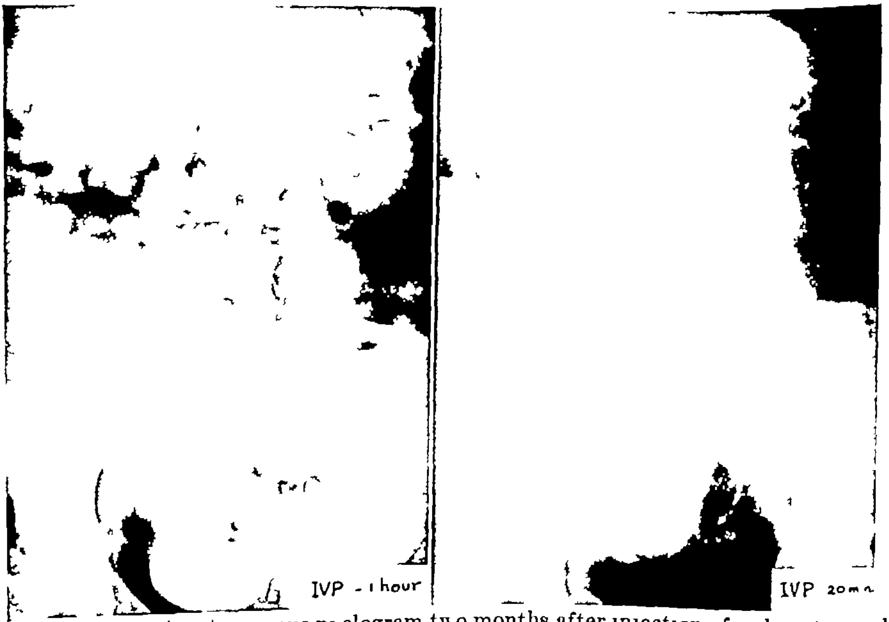

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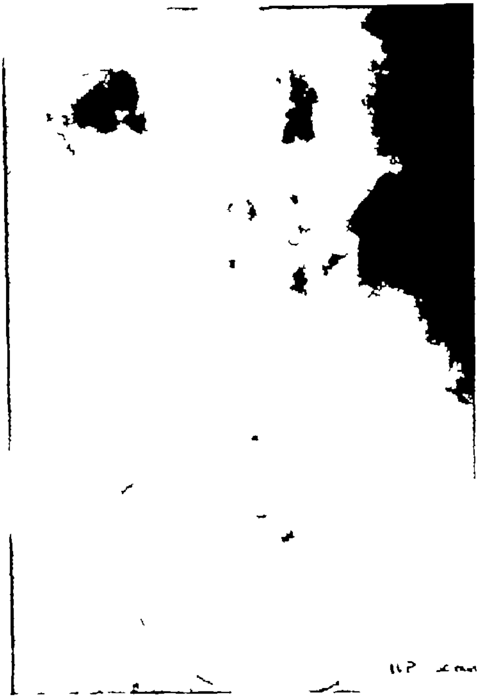

Fig 3 Case 3 Intravenous pyelogram one and one half years after gold injection demonstrates left ureteral obstruction just below pelvic brim

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May 7, 1954, 70 mc gold was injected into each parametrium in the usual manner On May 28, 1954, the final radium application (3240 milligram hours) was performed There were no symptoms of genitourinary tract disease following any of these procedures

In October 1955, the patient was hospitalized because of acute low back pain of ten days' duration The clinical impression was herniated intervertebral disc and there was a good response to conservative measures The gynecologist could find no evidence of recurrence of tumor X-rays of the spine and pelvis were negative for metastatic lesions The urinalysis was negative Intravenous pyelograms (fig 3) revealed a marked left hydronephrosis and hydroureter with the point of obstruction at the pelvic brim The ureter below this point appeared normal The right collecting system was normal Further urological evaluation was not requested

The patient has remained free of symptoms and without evidence of recurrence since this episode She returned for intravenous pyelograms in October 1956 at our request No change had occurred in the status of the upper urinary tract

Urological consultation was not requested in this case The patient had no history of pre-existing renal disease and no evidence of pelvic cellulitis after treatment The patient has been clinically free of tumor for two and one-half years The location of the ureteral obstruction was just below the pelvic brim and suggests that the radioactive gold injection rather than the radium application was responsible for the ureteral obstruction

Case 4 Cystitis and ureteritis B H No 241750, D W, a 37-year-old-Negro woman, was first hospitalized in August 1954 because of a yellow vaginal discharge No symptoms were referable to the genitourinary tract A cervical biopsy was reported as squamous cell carcinoma, Broders' type 2 The classifi-

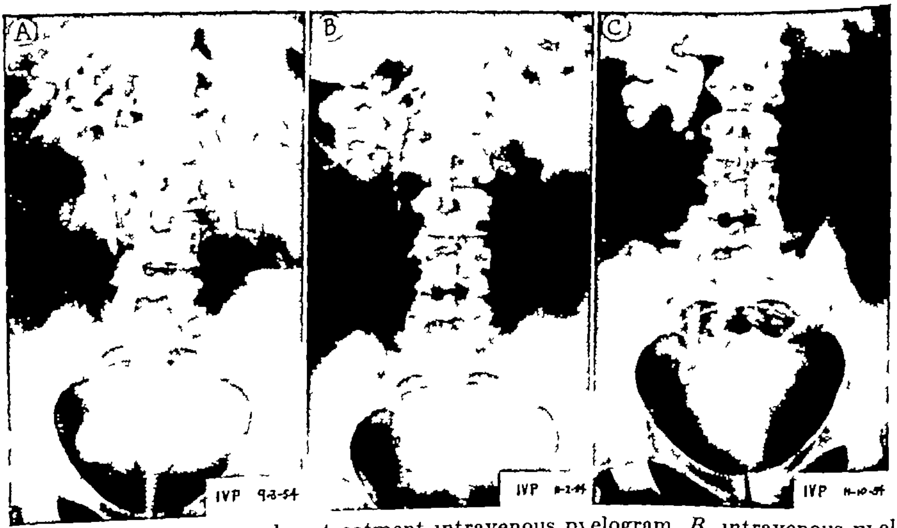

FIG 4 Case 4 *A*, normal pretreatment intravenous pyelogram *B*, intravenous pyelogram (one hour delayed film) six weeks after gold injection demonstrates nonvisualization of left kidney and right hydronephrosis *C*, intravenous pyelogram seven weeks after gold reveals progression of right hydronephrosis and deformity of left half of bladder shadow

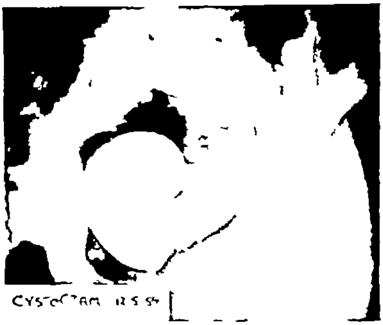

FIG 5 Case 4 Cystogram in right posterior oblique projection demonstrates urinary extravasation

cation was League of Nations stage 1 On September 3, 1954, a pretreatment intravenous pyelogram was obtained (fig 4, *A*) and interpreted as normal The five-minute film is illustrated and the compression blocks are in place Subsequent films in this series demonstrated prompt emptying of both collecting systems The following day, 60 mc radioactive gold was injected into each parametrium in the usual manner Immediately after this injection the patient complained of frequency, dysuria and left sciatica * Two weeks later, radium was applied in a colpostat (4180 mg hours) The recovery was uneventful but the urinary symptoms persisted

On October 30, 1954, the patient was readmitted for a Wertheim hysterectomy She still complained of dysuria and left sciatica Pelvic examination revealed marked induration of the left parametrium extending to the lateral pelvic wall A preoperative intravenous pyelogram (fig 4, *B*) revealed nonvisualization of the left kidney two hours after the injection of the contrast medium and delayed filling with hydronephrosis on the right A Wertheim hysterectomy with pelvic lymphadenectomy was done in November 1954 The surgeon encountered a hematoma in the left paravesical space A perforated ulcer, 3 cm in diameter, was noted on the left anterior wall of the bladder The edges of this ulcer were excised, the defect closed The bladder was drained by a suprapubic catheter and a ureteral catheter was passed easily to the left kidney and brought out through the cystostomy opening No tumor was seen in the gross specimen On the fifth postoperative day the ureteral catheter was pulled out by error and the temperature rose to 38 5°C Urological consultation was first requested at this time An intravenous pyelogram revealed progression of the right hydronephrosis and hydroureter, and distortion of the left lateral wall of the bladder (fig 4, *C*) By this time the suprapubic fistula had closed spontaneously and the patient was voiding The urological consultant recommended urinary diversion but the gynecologist felt that further observation was in order

One month later further urological study was requested because of the persistence of a low-grade temperature elevation A gravity cystogram (fig 5) demonstrated extraperitoneal urinary extravasation Cystoscopy disclosed a shaggy, necrotic left anterolateral bladder wall A ureteral catheter was passed to the left kidney pelvis with ease and remained indwelling for several days The temperature gradually returned to normal and the patient was then discharged approximately two months after her radical hysterectomy

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* Sciatica has been the most distressing neurological complication following the use of radioactive gold and will be the subject of a subsequent report

In January 1955, the patient returned to the hospital with a complaint of fatigability, frequency and dysuria She continued to have a low-grade temperature elevation Urine culture revealed Aerobacter aerogenes which was sensitive only to chloromycetin, but a clinical trial of this drug did not result in any improvement An intravenous pyelogram was repeated and was unchanged This time urologic opinion prevailed and an exploratory laparotomy was done Bilateral marked perivesical induration was present, more prominent on the left Urinary diversion was accomplished by anastomosing the ureters to an isolated segment of ileum The postoperative course was uneventful and the patient had immediate symptomatic improvement

The patient has been seen frequently in the outpatient clinics up to the time of this writing She feels well, has gained 30 pounds and has had no difficulty with the management of her ileostomy bag

In May 1955, an intravenous pyelogram was repeated (fig 6, *A*) Some regression of the right hydronephrosis was noted In addition there was evidence of visualization on the left which was quite definite on the original x-ray We were interested in the patency of the ureteroileal anastomoses and did a reflux ileogram A Foley catheter was inserted in the ileostomy and the balloon inflated The usual cystogram medium was then allowed to flow through the catheter by gravity and promptly regurgitated into both collecting systems (fig 6, *B*) indicating adequately patent ureteral orifices The most recent intravenous pyelogram one year after urinary diversion demonstrated additional return of "function" on the left (fig 6, *C*) The patient has remained clinically well since the ureteral transplantation and has no evidence of recurrence of her tumor

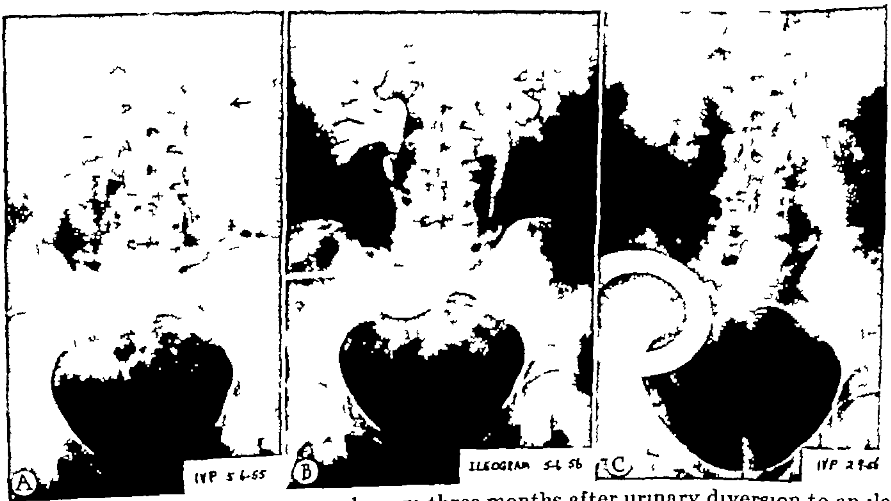

FIG 6 Case 4 *A*, intravenous pyelogram three months after urinary diversion to an ileal segment *B*, reflux ileogram obtained by instilling diodrast into ileostomy stoma through Foley catheter *C*, intravenous pyelogram one year after urinary diversi

COMMENT

One hundred and thirty-five patients received radioactive gold as part of the treatment of uterine carcinoma and 10 of these subsequently had significant complications involving the genitourinary system Certainly, in some patients delayed complications have developed but the patients have sought medical care elsewhere and therefore do not appear in this series Others may have partial or complete ureteral obstruction without symptoms and for that reason have not been investigated Many patients whose symptoms were mild, particularly with regard to cystitis, have not been studied Considering the probable additions to the group with demonstrated urologic disease, it still appears that extensive surgery and irradiation have been accomplished in this series of patients with a urologic morbidity of less than 10 per cent and a urologic mortality of less than 1 per cent

It is always difficult to pinpoint a single etiological factor responsible for urologic complications in a patient treated for carcinoma of the cervix because of the multiplicity of therapeutic agents involved Those patients in whom recurrent tumor was demonstrated have been eliminated from this discussion in order to limit the analysis to the role of the therapeutic agents Of course, it is well known that metastases from treated cervical carcinoma may not become apparent for many years after the initial therapy Perhaps some of the cases presented may ultimately develop tumor recurrence but at present all are considered to be cured There is a good likelihood that this is a valid assumption since the group happened to be limited to stage 1 and 2 lesions A single case of adenocarcinoma of the cervix had a Wertheim hysterectomy and no positive lymph nodes were demonstrated

In most of the cases then, the task is to place the blame on the radioactive gold injection as distinct from the radium application During the case presentations several factors were emphasized which seem to indicate that the radiogold was actually primarily responsible for the urologic complications In four cases the symptoms of bladder irritation began immediately after the gold injection In two cases the association of cystitis with sciatica pointed to the role of the radioactive gold In three patients, the point of ureteral obstruction demonstrated was just below the pelvic brim, that is, several centimeters above the usual site of radiation ureteral injury from conventional radium applications[9] In three cases the location of the radiation cystitis was on the anterior and lateral wall of the bladder rather than the bladder base or retrotrigonal area This combination of findings has led us to the conclusion that the radioactive gold injection was the main source of difficulty

Pelvic cellulitis not infrequently follows high dosage radiation therapy to the cervix This was the clinical diagnosis in three of our ten cases Therefore, infection might be considered as the primary factor in the etiology of ureterectasis However, several instances of pelvic cellulitis in this series have occurred without pyelographic or cystoscopic evidence of urinary tract disease In addition, it was the clinical impression in these three cases that the pelvic cellulitis was a direct result of the radioactive gold injection

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[9] Mansur, E E The ureter and its involvement in pelvic irradiation Radiology, 42 147 1944

The characteristics of radiation cystitis encountered in this series were in no way different from the cystitis described by others resulting from the use of radium[10] [11] Only the location of the lesion in the bladder was different In discussing the typical delayed cystitis after the use of radium, Dean stated that "radiation ulcer is always located on the posterior third of the bladder base and almost always in the midline Large ulcers have been seen extending upward on the posterior wall, but I have never found involvement of the trigone, anterior or lateral walls"[12] In our cases, the irradiation ulcer was located on the lateral wall of the bladder The therapeutic challenge presented by this complication still remains[13] [14] It is of interest that one patient was dramatically benefited by the use of a uterine curette to remove the calcareous surface of an ulcer

Several authors have reported fatal bilateral hydronephrosis following irradiation of cervical carcinoma without demonstrable tumor at autopsy[15] [18] On the other hand, some have doubted the existence of ureteral obstruction from radiation injury alone and without evidence of metastatic tumor[19] A consensus of recent literature[20] [21] would seem to agree with Spence who stated that "close analysis of reported cases reveals that although there are occasional exceptions, most of these reported as having stricture due to radiation progressed to death with tumor in the broad ligament Ureteral obstruction above the intramural portion of the ureter is primarily due to parametrial extension of the neoplasm"[22]

Spence also stated that "since the cause of ureteral obstruction is tumor in the broad ligament, the problem is insoluble by the urologist and must await improved radiation techniques which will rid the broad ligaments of obstructing growth" The use of a radiation source that has been injected directly into the parametrium has evidently altered some of these concepts Case 4 is a good example of radiation periureteritis The fact that this was an early lesion and

[10] Dean, A L Injury of the urinary bladder following irradiation of the uterus J Urol, 29 559 1933

[11] Graves, R C, Kickham, C J and Nathanson, I T Bladder complications of the treatment of carcinoma of the cervix Surg, Gynec & Obst, 63 785, 1936

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[15] Everett, H S Urological complications following pelvic irradiation Am J Obst & Gynec, 28 1, 1934

[16] Everett, H S The effect of carcinoma of the cervix uteri and its treatment upon the urinary tract Am J Obst & Gynec, 38 889, 1939

[17] Schmitz, H Complications in urinary tract due to carcinoma of the uterine cervix or irradiation treatment Am J Roentgenol, 24 47, 1930

[18] Smith, G G and Leadbetter W F Effect of irradiation on lower ureters Tr Amer Assn Genitourin Surgeons, 35 195, 1942

[19] Beach, E W Urologic complications of cancer of the uterine cervix J Urol 68 178, 1952

[20] Valk, W L Urological complications of carcinoma of the cervix J Urol, 47 686, 1942

[21] Hoffman, D E Ureteral obstruction following irradiation treatment of cancer of the cervix West J Surg, Gynec & Obst, 50 69, 1942

[22] Spence, H M and Hare D M Ureteral obstructions associated with carcinoma of the cervix J Urol, 62 219, 1949

that no tumor was demonstrated in the specimen removed by Wertheim hysterectomy and pelvic lymphadenectomy makes the likelihood of persistent tumor very slight.

The need for more active participation by the urologist in the evaluation of patients with carcinoma of the uterine cervix has been made before.[23] This study further emphasized this need. As a result of some of our early urologic difficulties all patients who are now to receive radioactive gold have a more complete pretreatment urologic evaluation. Finally, we have become convinced of the value of routine pyelographic study after treatment and of the advisability of prompt surgical intervention and urinary diversion in the presence of significant bilateral ureteral obstruction.

SUMMARY

The records of 135 patients with uterine carcinoma treated by the injection of radioactive gold into the parametrium have been analysed. The records of several of the patients with urological complications have been presented.

A technique for retrograde filling of the upper urinary tract in patients with ureteral diversion to an ileal segment has been mentioned.

The author wishes to thank Drs. Willard Allen and Alfred Sherman for permission to use the material provided by their patients and particularly for their close co-operation in the analysis and presentation of this material.

607 N. Grand Blvd., St. Louis, Mo.

[23] Colby, F. H. Urinary-tract complications from uterine cancer. New Eng. J. Med. 229: 231, 1943.

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SUMMARY

The records of 135 patients with uterine carcinoma treated by the injection of radioactive gold into the parametrium have been analysed The records of several of the patients with urological complications have been presented

A technique for retrograde filling of the upper urinary tract in patients with ureteral diversion to an ileal segment has been mentioned

The author wishes to think Drs Willard Allen and Alfred Sherman for permission to use the material provided by their patients and particularly for their close co-operation in the analysis and presentation of this material

607 N Grand Blvd, St Louis, Mo

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THE STANDARDIZED COLUMBIA UNIVERSITY CYSTOGRAM

ARCHIE L DEAN, JR , JOHN K LATTIMER AND CORNELIA B McCOY

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In evaluating the success of treatment in children with dilated urinary tracts, cystograms are frequently taken before and after therapy and compared to see whether improvement has occurred This examination is of great value However, if the contrast medium is not injected with identical pressures each time and by the same technique each time, comparisons of even the simplest cystograms will not be valid In the past, at this hospital, cystograms were made by filling the bladder with radiopaque material until the patient complained of feeling full, then the radiograms were taken Difficulties in interpretation of the resultant studies arose because of varying degrees of filling of the bladder Because of the lack of a standardized technique, postoperative followup examinations were not comparable Accurate comparisons of cystograms made at different clinics also were not possible (fig 1)

As a first step towards achieving consistent pictures, we felt that we needed a standardized technique for a simple cystogram which incorporated the advances suggested by Stewart, Roth and others, such as the delayed film and the addition of antibiotics to the contrast medium, for example It should be clearly understood that it is desirable that each film be inspected as it is developed so that additional special films can be added if special indications are seen For instance, the "squat shot" of Boyce and Vest may show the lower ureters, or films taken during voiding may show reflux only at that time, or massage of the filled bladder may cause reflux, or the addition of "floating lipiodal" may demonstrate partial impairment of bladder efficiency As a further method of investigation, cystograms may be made by instilling a small amount of radiopaque fluid into the bladder, and allowing the bladder to fill slowly, by the natural accumulation of urine, as suggested by Stewart These pictures may add further information and are likely to show bladder sizes different from those shown by any standard pressure technique However, if this technique is the only one used some lesion may be missed, as shown in case 4 Moreover, this technique requires repeated x-ray exposures at 15 to 30-minute intervals for as long as two or three hours Such lengthy examinations are not feasible as routine procedures for every cystogram They can be added when indicated

The purpose of this report is to describe a practical, rapid, standardized cystogram technique now utilized on the Babies Hospital service of the Squier Urological Clinic This method includes several measures directed at revealing the presence or absence of impaired drainage Over one hundred of these examinations have been performed without any untoward reactions

Read at annual meeting, American Urological Association Pittsburgh, Pa , May 6-9, 1957

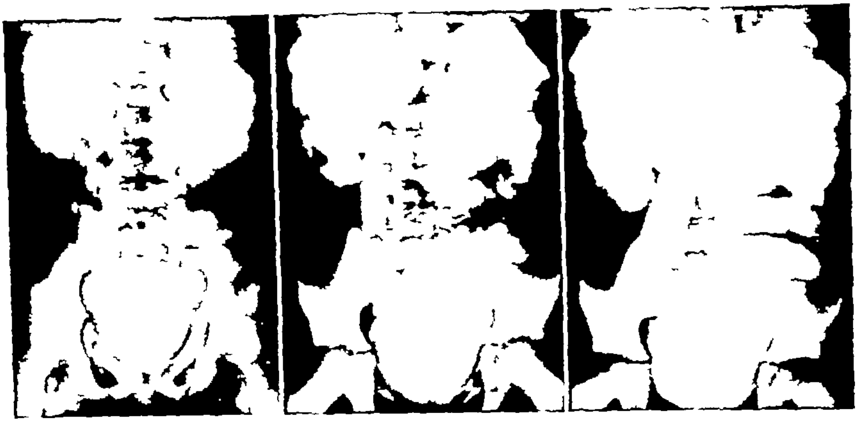

FIG 1 Three cystograms performed on same patient On left container of contrast medium was hung exactly 12 inches above symphysis pubis of patient and fluid allowed to drip into bladder by gravity Cystogram taken when the drip stopped The procedure was repeated with the reservoir at 24 inches (60 cm) in center photograph and at height of 36 inches in the film on right Renal pain occurred with the reservoir at 36 inches

METHOD

A small urethral catheter is inserted into the patient's bladder while the child is still among familiar surroundings in his bed or on his ward The catheter may be either taped in place or a small Foley catheter may be used Several minutes later the child is taken to the radiology department where the cystogram is to be performed A material which we have found satisfactory to instill into the bladder for this purpose is a mixture of two ampules of hypaque[1] (30 cc each) aseptically mixed with 200 cc sterile isotonic saline The saline is obtainable in aseptic previously prepared disposable flasks containing 250 cc 50 cc of which are discarded Plastic disposable tubing which has a threaded cap at one end, available under the trade name of venopak is then screwed to the top of the flask as for an intravenous infusion The tip of the plastic tubing is attached to the cleaned end of the urethral catheter, and the flask is hung from a pole exactly 24 inches (60 cm) above the symphysis pubis of the patient We have found that higher pressures may cause kidney pain in patients with reflux and that lower pressures may give inadequate filling

Immediately before beginning the flow of radiopaque fluid into the bladder, 500 mg neomycin is injected into the tubing This helps to avoid febrile reactions The hypaque mixture is then allowed to drip into the patient s bladder at a rate of 120 drops per minute In the case of infants, we routinely send a bottle of formula with the patient to the radiology department The patients are given formula while the bladder is being filled This not only quiets the child but distends the stomach with gas so as to better outline the kidneys When the intravesical pressure increases to such an extent that the fluid no longer runs into the bladder, the catheter is clamped and an x-ray is taken If vesicoureteral reflux

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[1] Hypaque sodium brand of diatrizoate sodium sterile 50% aqueous solution Winthrop Laboratories New York N Y

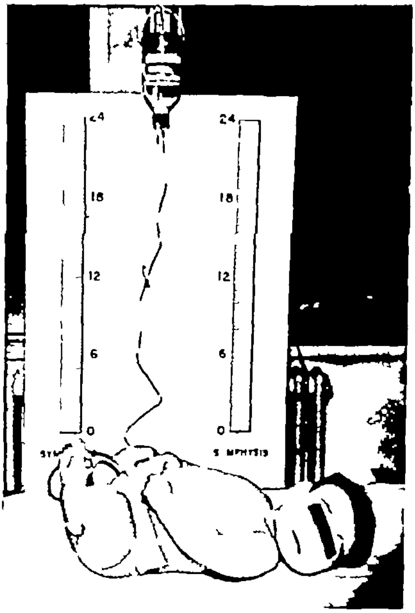
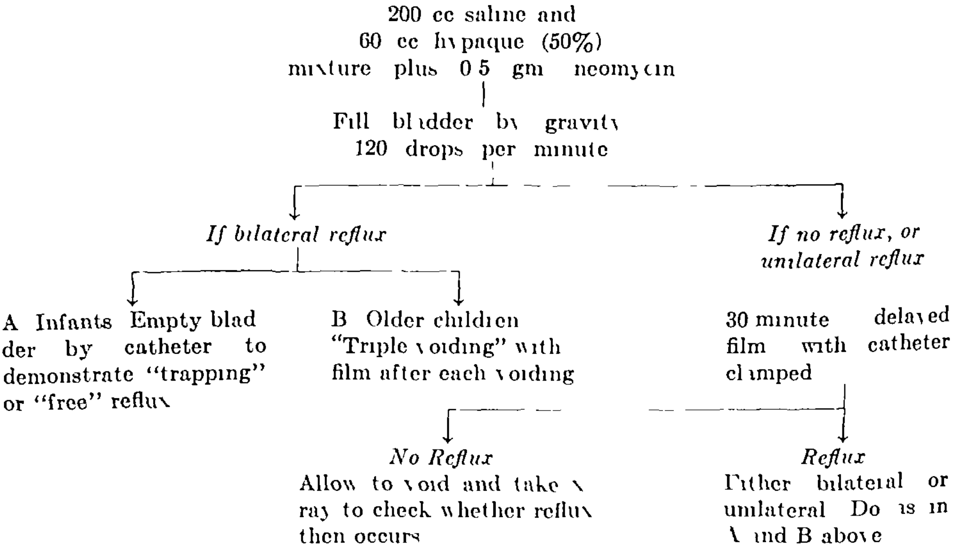


FIG 2 Cystogram in progress The contrast medium is in a container twenty four inches (60 cm) above the child's bladder

TABLE 1 *Technique of gravity cystogram*



200 cc saline and
60 cc hypaque (50%)
mixture plus 0 5 gm neomycin

Fill bladder by gravity
120 drops per minute

If bilateral reflux

A Infants Empty bladder by catheter to demonstrate “trapping” or “free” reflux

B Older children “Triple voiding” with film after each voiding

If no reflux, or unilateral reflux

30 minute delayed film with catheter clamped

No Reflux
Allow to void and take x ray to check whether reflux then occurs

Reflux
Either bilateral or unilateral Do as in A and B above

occurs an attempt is made to determine whether “trapping” is present in the ureters In infants this is most easily determined by opening the urethral catheter and draining the bladder for ten minutes, followed by a second x-ray exposure If no residual opaque material is visualized in the kidneys or ureters, then it is ar t no significant ureteropelvic or ureterovesical obstruction is present ll seen, additional films are taken to determine how long it takes for complete evacuation In older children who can void on command (after bilateral vesicoureteral regurgitation is demonstrated) the catheter is removed and the patient instructed to void An x-ray is taken and then the patient is urged to walk around the bathroom and to void twice more, at intervals of one minute, with x-rays taken after each voiding Some children with ureteral reflux will completely empty dilated ureters and kidneys of radiopaque material by such triple voiding

If no reflux is present on the first film or if the vesicoureteral reflux is only unilateral the catheter is clamped for about thirty minutes and a repeat x-ray is taken in an attempt to demonstrate delayed ureteral reflux Even if no regurgitation is found after this delay a post-voiding" x-ray at this time may demonstrate vesicoureteral regurgitation Figure 2 illustrates the cystogram apparatus Table 1 explains the plan of procedure

ILLUSTRATIVE CASES

Case 1 (No 235578) An 8-month-old male child was transferred to the Babies Hospital from another hospital because of recurrent fever of unknown etiology An excretory urogram was performed the day prior to transfer by making a cut down on the child's ankle vein Although function was poor, faint visualization suggested bilateral hydronephrosis On the day of admission a gravity cystogram was performed It clearly outlined bilateral hydronephrosis and bilateral ureterovesical junction stenosis (fig 3) The child has improved following bladder neck resection and ureteral meatotomies

Case 2 (No 906717) The patient was one of 9-year-old identical twin boys, both of whom had dilated bladders and bladder neck contractures This boy underwent retropubic bladder neck resection and right ureteral meatotomy because of stenosis of the right ureter at the ureterovesical junction The boy voided with a good stream thereafter but on occasion he noticed fever and right flank pain associated with efforts at retaining his urine for longer periods than usual A cystogram revealed right vesicoureteral regurgitation Triple voiding radiographs suggest that he empties his kidney by this maneuver, and he has been instructed to void in this fashion while at home (fig 4)

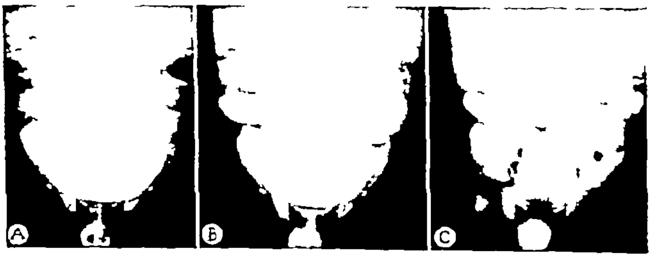


FIG 3 Case 1 *A* gravity cystogram reveals large bladder No evidence of ureteral reflux. *B* after 30 minutes with catheter clamped bilateral vesicoureteral regurgitation is demonstrated *C* film taken 10 minutes after bladder was emptied by opening catheter Bilateral ureterovesical stricture is demonstrated by x ray This was later confirmed by surgery

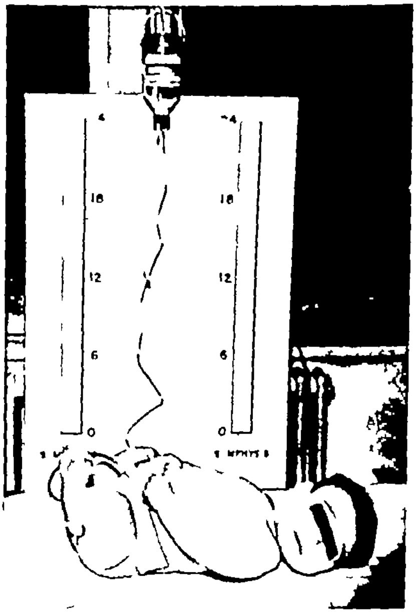


FIG. 2. Cystogram in progress. The contrast medium is in a container twenty four inches (60 cm.) above the child's bladder.

TABLE 1. *Technique of gravity cystogram*

200 cc. saline and
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No Reflux
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Reflux
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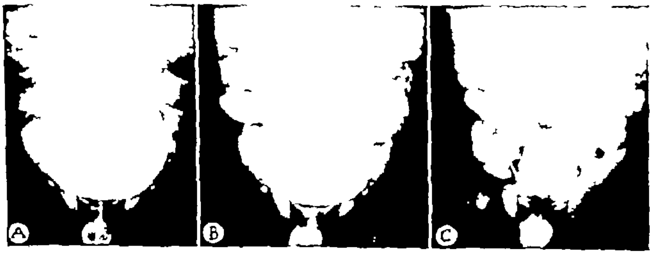

FIG 3 Case 1 A gravity cystogram reveals large bladder No evidence of ureteral reflux *B*, after 30 minutes with catheter clamped bilateral vesicoureteral regurgitation is demonstrated *C* film taken 10 minutes after bladder was emptied by opening catheter Bilateral ureterovesical stricture is demonstrated by x ray This was later confirmed by surgery

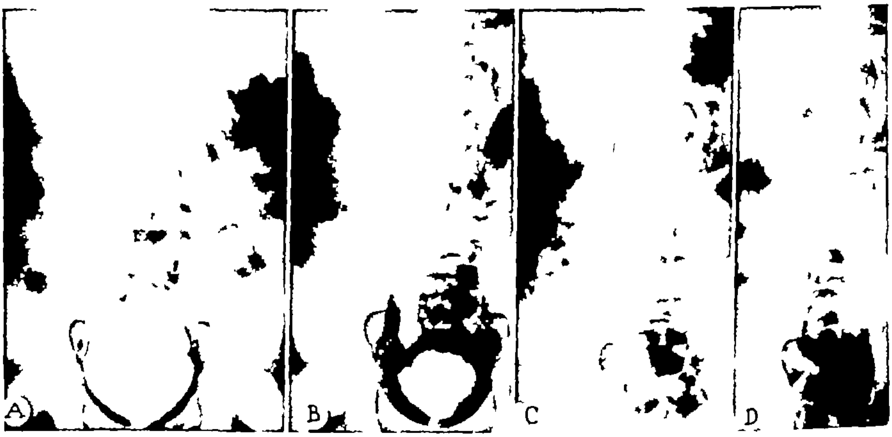

FIG 4 Case 2 A, immediate gravity cystogram reveals right vesicoureteral reflux No reflux present on left B, after first voiding bladder, ureter, and kidney empty somewhat Still no left vesicoureteral regurgitation C after second voiding, bladder is practically empty and right kidney has only a small residual D, after third voiding, kidney is emptied of opaque material

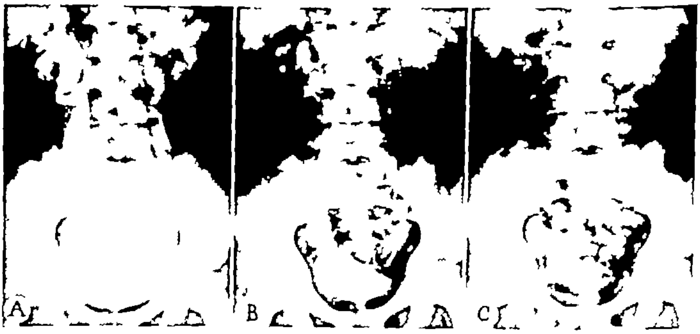

FIG 5 Case 3 A, immediate gravity cystogram reveals full bladder and bilateral reflux, more on right B, after first voiding, most of contrast medium has been cleared from kidneys and ureters C, after second voiding bladder and upper tracts are empty

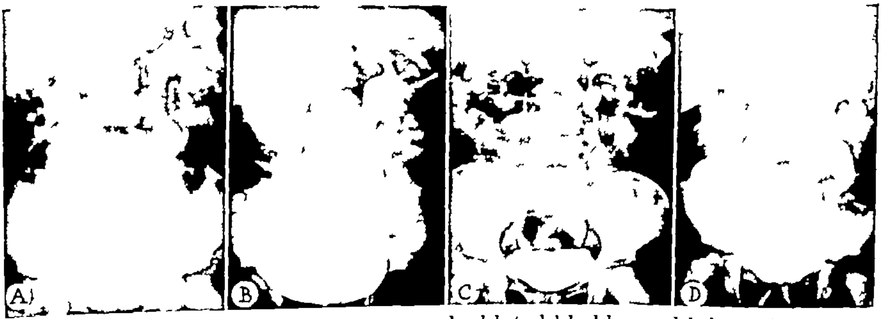

FIG 6 Case 4 A, excretory urogram reveals dilated bladder and bilateral hydroureter and hydronephrosis B, gravity cystogram reveals immediate bilateral vesicoureteral regurgitation C, after three months of bladder drainage by means of indwelling urethral catheter, catheter was removed and six weeks later another excretory urogram revealed normal bladder capacity and only minimal hydronephrosis D, gravity cystogram performed at this time, however, still demonstrates bilateral vesicoureteral regurgitation and bilateral hydronephrosis Followup studies indicate that child s bladder is beginning to enlarge again

Case 3 (No 248982) A 9-year-old girl had pyuria and fever for several years She was known to have had bilateral hydronephrosis but no bladder neck stricture had ever been demonstrated Gravity cystograms and triple voiding radiographs demonstrate bilateral vesicoureteral reflux and also show that the patient can empty her kidneys and ureters by triple voiding She has likewise been instructed to perform this while at home (fig 5)

Case 4 (No 232596) A 2-year-old girl had had fever and pyuria for several months Her blood chemistry determinations were normal, but she was pale and poorly nourished An excretory urogram revealed a large bladder and bilateral hydronephrosis (fig 6) No neurological abnormalities were present and panendoscopy revealed no bladder neck disease other than loose folds of mucous membrane about the bladder neck The child was treated by means of an indwelling Foley urethral catheter for a period of three months Six weeks after removal of the catheter a repeat excretory urogram and gravity cystogram were made Although the intravenous urogram revealed much improvement, the cystogram showed that bilateral vesicoureteral regurgitation still could be demonstrated Thus far the child has shown no recurrence of the fever This case serves to emphasize the fact that a normal or near normal excretory urogram can mask changes which are easily uncovered by the cystographic technique It also suggests that in some children, reflux is not dangerous if bladder neck resistance is overcome It further demonstrates that the cystogram performed by this standardized technique is reproducible

DISCUSSION

For us, the cystogram has been of great diagnostic importance in the treatment of children with chronic urinary tract disease It is felt that by standardizing the technique, however, we are better able to follow our patients and to compare with more accuracy the effectiveness of various new operative procedures In addition, we believe that if other institutions were to adopt a standardized cystogram technique, comparisons of x-rays taken at these different institutions would be much more valuable

The cystogram is useful not only for demonstrating vesicoureteral regurgitation, but it also may demonstrate areas of impaired drainage in these cases These can easily be shown by opening the urethral catheter and allowing the bladder to drain for ten minutes A film taken at that time will show whether there is residual urine in the ureters or pelves An alternative method which can be used in older children and adults is the triple voiding technique which will reveal ureteral retention or "trapping," if it is present We have found that the triple voiding technique is also a valuable aid in the therapy of children with dilatation of urinary tract

It should be recognized that the technique described here employs retrograde filling of the bladder to a standard pressure and that still more information may be obtained by additional techniques which are described and which can be used for special cases

SUMMARY

A standardized gravity cystogram technique is presented The materials used for this method are easily available to all urology and radiology departments The advantages of this technique are that it is quick, aseptic, and can easily be standardized so that cystograms might be compared between different hospitals just as intravenous pyelograms are now comparable Emphasis on the "trapping" film has been stressed in order to reveal the presence or absence of obstructive lesions Additional special views or techniques may be added if special indications arise The triple voiding cystogram is demonstrated and its usefulness in the diagnosis and treatment of patients with vesicoureteral regurgitation is indicated

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RECENT ADVANCES IN CYSTOSCOPIC PHOTOGRAPHY PRESENTATION OF NEW EQUIPMENT

LOWRAIN E McCREA

Endoscopic photography was introduced in 1940 and has now been definitely established as an important adjunct to the medical profession Since the development of prismatic endoscopic photography other fields of medicine notably bronchoscopy, have successfully utilized photography in the demonstration of various lesions particular to that section of medical practice Investigators interested in other fields of medicine have now inaugurated experimentation which, it is hoped, will result in the perfection of equipment suitable to their individual requirements It is believed that photographs produced by present day prismatic endoscopic equipment are of an inestimable value as visual records, not only to the physician but to the patient as well It is the purpose of this presentation to tender new equipment, capable of instantaneous photographic exposures on both black and white and color film

Visualization of the different canals and cavities of the human body has been attempted since the dawn of medical practice It is an established historical fact that the ancient Hebrews were the first to use the vaginal speculum, and that rectal specula have been found in the ruins of Pompeii Body cavities having large orifices were the only recesses that could be explored Examination of these cavities was always limited, due to cumbersome equipment which precluded any attempted exploration of those body recesses with small orifices It was not until Bozzini (1805) introduced the *licht-leiter* that attempted examination of the urethra was made possible The results attained by this equipment were not good, but it was the first successful attempt to explore the organs of the genitourinary tract Unfortunately, Bozzini's contribution was not favorably received before the Vienna Medical Academy His work even aroused the ire of the Austrian Government, which charged the Academy to investigate the radical instrument with which he, Bozzini, attempted to explore ' the hidden recesses of the body " After considerable deliberation and investigation, the Faculty of the Academy announced that the contrivance was little more than a toy and intimated that Bozzini displayed undue curiosity in attempting to investigate the hidden recesses of the body ' Following Bozzini's original work, many attempts at cystoscopy and exploration of the bladder by instrumental means were made

It was not until 1887 that Max Nitze, and Leiter, working independently, introduced a cystoscope with an optical system Nitze continued his experimental work and in 1894 attempted to photograph the interior of the bladder As the photographs produced were not clear, and the image was distorted, the equipment was quickly abandoned Since that time numerous instruments for cystoscopic photography have been conceived and advanced by many observers It is surprising to learn of the number of investigators who have envisioned the value

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Read at annual meeting of Mid Atlantic Section of American Urological Association Virginia Beach Va March 21-24 1957 of the endoscopic photograph and who, for one reason or another, became disgusted with their investigation, admitted failure, and unfortunately discarded their unfinished work

In 1940, it was a personal privilege to present to the profession equipment suitable for black and white photography within the bladder of the living human In 1942, equipment capable of photography of intravesical lesions in natural color was presented This equipment, although efficient to a degree, was capable of taking photographs only by time-exposure The lighting facilities of this equipment could never be perfected to that degree which would permit instantaneous photographic exposure on color film Continuous experimental work by competent electrical and lighting engineers could never produce an electric bulb of low wattage, capable of sufficient lighting qualities to permit instantaneous photographic exposures Electric light bulbs of higher voltage were used experimentally, but the danger of shock to the patient was always present and they were discarded Realizing that low voltage bulbs were not feasible to produce sufficient light for intravesical photography, the field of indirect lighting by quartz rod was explored

Indirect lighting by quartz rod transmission has been used for many years in mechanical and engineering fields, but only recently has the principle been applied to endoscopic examination of the patient French investigators have recently successfully used the technique of quartz rod light transmission in many fields of prismatic endoscopic medical photography Of these investigators, Jaupitre has perfected and used, in both stills and movies with color film, such equipment for intravesical photography It was following the successful use of such principle by the French investigators that this principle was modified and adapted for use in the camera herein presented

Utilizing the indirect lighting of the quartz rod technique, a reflex cystoscopic

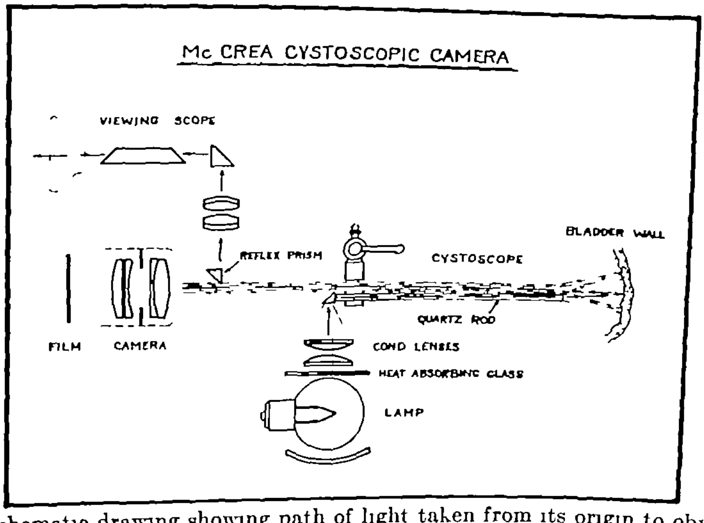

FIG 1 Schematic drawing showing path of light taken from its origin to object photographed back to film of camera and then through continuous visual reflex

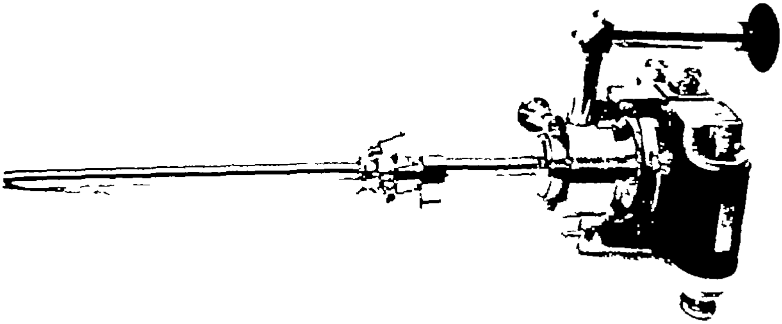

FIG 2 Sheath and lens system attached to camera Camera a Robot Royal, is used because of film advancing mechanism Note position of continuous visual reflex

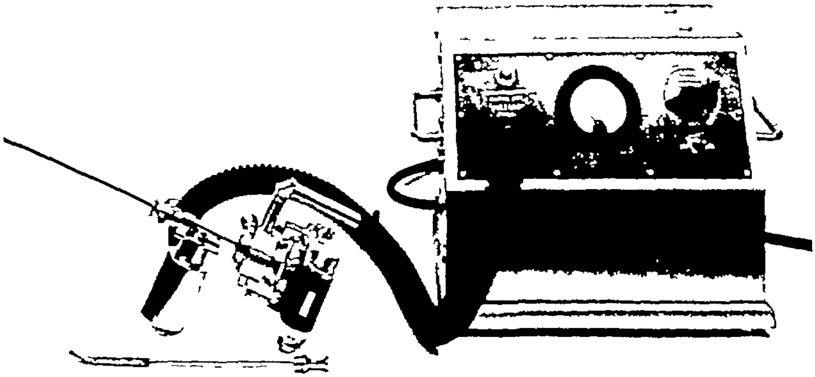

FIG 3 Camera with control unit for light intensity and blower system for cooling lamp

camera and lens system was constructed which permits the taking of instantaneous intravesical photographs in color The lens system, at present, is a direct, forward lens As experimentation continues, lenses of other angles will be used Granted, the lens and lighting system as is presently used is good for only one purpose, namely, photography, but other applications of the equipment with optics of other angles are in the realm of possibility (fig 1)

The photographic detail and quality of both black and white and color transparencies, as portrayed by this lens equipment, are excellent With such sharpness of photographic detail, enlargements should be of excellent photographic quality The reflex of the camera is so arranged that visualization of the photographic field is constantly observed during actual photographic exposure By such arrangement, any motion or momentary loss of the photographic field may be instantly followed by another and proper exposure The camera mechanism used is a Robot with automatic advance of the film following exposure A system that has been advocated since 1942 (fig 2)

The light utilized is from an air-cooled electric bulb emitting an intense white light (fig 3) The light is projected through a quartz rod by being angularly reflected from one surface of the rod to the other surface until it escapes at the exit end The quartz rod used in this equipment is 2 75 mm (110 inch) in diameter With the proper concentration of the light beam and the surface treatment given the quartz, projection of a powerful white light onto the subject permits brilliant photography The entrance and exit ends of the rod are angled to a predetermined angle to accept the greatest amount of incoming light and to beam the outgoing light angularly to the surface area covered by the visual field of the cystoscopic telescope

The fluid to which the quartz rod will be subjected within the body or by normal sterilization will not affect the surface finishes as quartz, particularly the fused material, is virtually immune to all acids except hydrofluoric, and to phosphoric acid at 150°C or above Alkaline solutions attack quartz very slowly and usually then at elevated temperatures

There are two highly important factors in intravesical photography, and unless due cognizance is taken of these factors, natural color photography will result in failure These two factors are 1) proper light and 2) the presence of a clear, sparkling, distending medium The most important of these two factors is proper light The light must be true white and brilliant to such intensity as will expose color film properly It is generally known that color film (kodachrome F) operates most efficiently at 3800° Kelvin It has been established that the intensity of light delivered by this equipment is 3800° Kelvin Such a ratio makes a perfect balance between light for proper exposure of the film and the output of light by the quartz rod The second important factor necessary to produce sharp photographic images is a clear, distending medium through which the light rays may pass without distortion Intravesical photographs must, of necessity, be taken through a distending fluid medium, and although all fluids distort or deflect light rays, it has been found that sterile distilled water causes less deflection than does any other fluid The presence of blood, pus, or other cellular debris, so frequently observed in pathological conditions of the bladder, will cause distortion of the image and deflection of the light rays with the production of a hazy, ill-defined photograph Preliminary irrigation of the bladder is imperative, until the irrigating fluid returns clear, particularly without the presence of blood, if a photograph of true color value is to be obtained The gradation in color of the vesical mucosa is of vital importance in the interpretation of many lesions To be able to photographically reproduce not only the physical outline of a lesion but to depict its actual color value and its gradations is of inestimable value and can only be reproduced by meticulous attention to detail

The photographic images obtained by this equipment are 7 mm in diameter The images are photographically sharp in detail, project readily and may be easily enlarged for printed illustration Such photographs, used either as a record of a vesical lesion, in the teaching of students or as text-book illustrations, present facts and factors beyond the scope of the spoken work or the most skillful drawing To visualize and to learn the fundamental nature of either the normal or the pathologic is a sound basis of good medical practice and also sound teaching whether the students are undergraduates or in advanced fields It is believed that the adaptation and routine use of such equipment will do much to promote better understanding of the behavior of many pathological processes

By the perfection of this equipment it is now hoped that many of the secrets of the canals and recesses of the human body may be fully revealed to the student of medical practice by the portrayal and study of many diseases made through the interpretation of actual accurate endoscopic photographs by an ever increasing number of competent physicians

I am deeply indebted to Mr E E Baker development engineer of light and optics for his wise counsel advice and interest in the fundamental construction and development of this equipment to Mr Henry N Pilling president of George P Pilling and Son Co surgical instrument manufacturer for his untiring effort in the construction of the lighting equipment capable of producing sufficient light for instantaneous photographic exposures and last but not least to Mr Harry S Rubens executive vice president of The National Electric Instrument Co for his unselfish co-operation design and construction of the lens and endoscopic sheath used in this equipment Without mutual understanding of the many personal and mechanical difficulties this work could never have been accomplished without their aid

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COLORED MOTION PICTURE PHOTOGRAPHY AND BLACK-AND-WHITE TELEVISION OF THE HUMAN URINARY BLADDER AND OTHER INTERIOR BODY ORGANS

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For many years past American instrumental urology has had the advantage of collaboration with a group of scientists The result of this fortuitous collaboration has been that American instrumental urology leads the rest of the world Nowhere has this been so spectacularly illustrated than in this, the latest result of such collaboration, namely, television of the urinary bladder and colored motion pictures of the same organ

Adequate telescopic systems have been available for visual inspection and diagnosis of conditions within the bladder and the urogenital system Foremost among these instruments has been the McCarthy panendoscope which utilizes, as its basic component, a foroblique telescope in conjunction with other accessory right angle and retrograde telescopes for visualization of conditions at the bladder neck Illumination has been provided by miniature tungsten coil lamps of high efficiency in relation to their diminutive size This illumination has been adequate for visualization and diagnosis Under ideal conditions it has been suitable for black-and-white photography using exposures up to 1½ seconds and for color photography where exposures of from 4 to 5 seconds were possible Extensive experimentation has been conducted over a number of years using miniature lamps having heavy tungsten filaments, which could operate at higher voltages for shorter periods of time, and also accessory lamps which could be flashed by overloading voltages These efforts resulted in a reduction in the exposure time required for black-and-white or color photography, but were not practicable because the benefit obtained in lesser time exposure was offset by the necessity for frequent lamp change and accessory equipment for overloading voltages

Other efforts were made to provide concentrated light source by means of point source zirconium tubes, capacitor discharge type lamps, and similar illumination systems The illumination provided by these light sources was more than adequate for colored motion picture photography or black-and-white television, but they were not practicable because of dangerous voltages required for their operation

The illumination of internal body cavities by means of light transmitting materials such as glass rods, quartz rods, and plastic rods has been advocated by numerous investigators, and some of these methods have found limited application The use of a glass rod as a light transmitting medium was first suggested by Smith in 1899[1] who described a surgical light using the principle of total reflec-

Accepted for publication June 3, 1957

[1] D D Smith, U S patent No 624 392 May 2, 1899

[2] Isacc J Smit, U S patent No 1,326,300 December 30, 1919

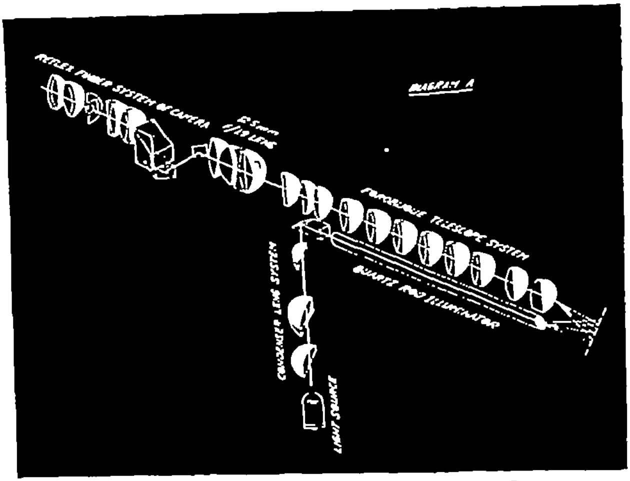

FIG 1 Optical system using motion picture reflex camera

tion through a transparent glass rod fitted with a light bulb located at the proximal end of the rod In 1919, I J Smit[2] described a surgical device in the form of a sound which utilized a transparent glass rod to transmit light from an incandescent bulb to interior body cavities Kerr[3] described a fused quartz transilluminator designed primarily for illuminating the human eye, having a fused quartz rod attached to a diagnostic set battery handle, with a small incandescent bulb placed at one end of the rod Hollnagel[4] described an illuminating unit for surgical work which consisted of a fused quartz rod, the outside of which was coated with silver and illumination for which was supplied by an incandescent bulb, which provided a light transmitted through the quartz rod to the distal end Leiter[5] described a cystoscopic unit, illumination for which was supplied by a glass optical system activated by an external incandescent lamp Thompson[6] described a safety light consisting of a fused quartz rod encased in a metal tube illuminated by an external incandescent lamp During the World War II period, the light conducting properties of plastics such as methyl-methacrylate (lucite) were used in military fire control instruments to provide edge illumination for reticles and for other military purposes Shortly after the end of World War II a number of devices for internal illumination were provided which utilized lucite for transmitting light supplied by external incandescent sources

In 1947, a number of experiments were conducted and experimental cystoscopic equipment was produced which provided a means by which light from a powerful external incandescent lamp could be conducted to the distal end of the system, utilizing methacrylate or quartz rods In such systems the light generated by the incandescent source was collected by an optical condensing system, and transmitted through the tube to the distal end of the instrument This equipment

[3] Charles H Kerr U S patent No 1 662 150 March 13 1928
[4] H P Hollnagel, U S patent No 1,706 161 March 19, 1929
[5] Friedrich F Leiter U S patent No 1 692 554 November 20, 1928
[6] J L Thompson U S patent No 1,965,865 July 10 1934

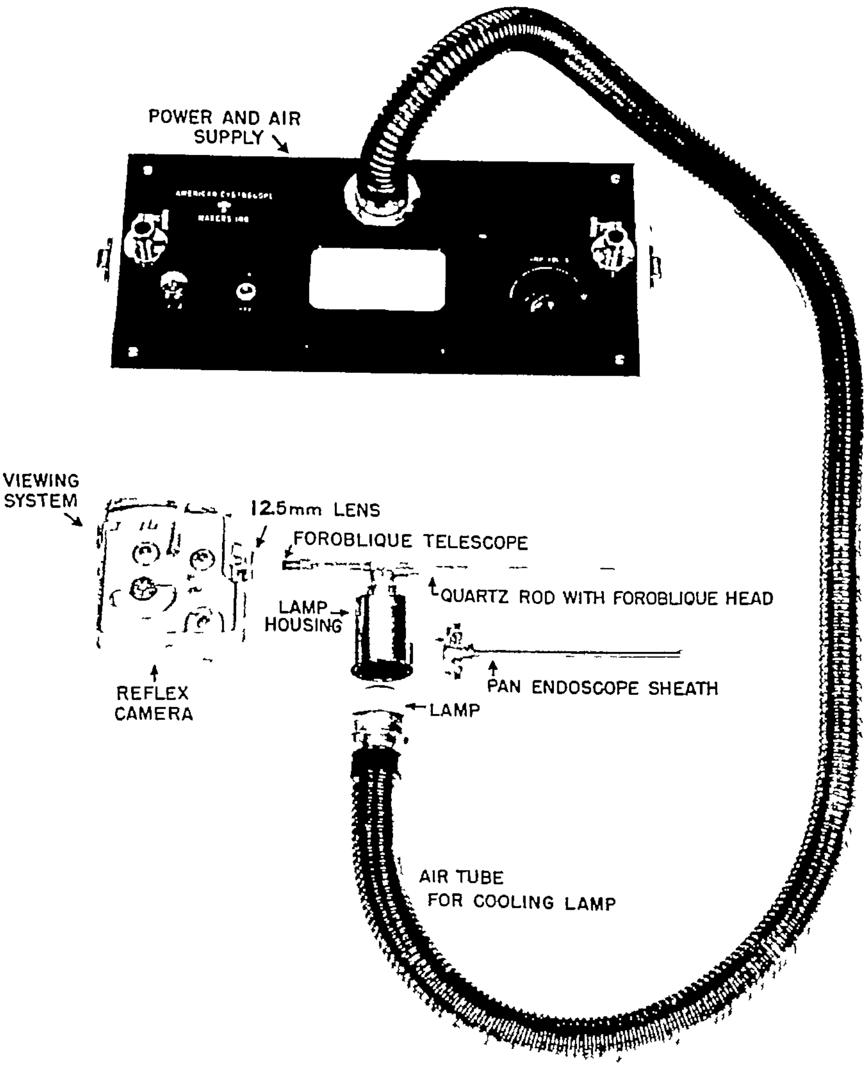

FIG 2 Composite photograph showing quartz rod panendoscope, sheath, reflex camera and power source

provided superior illumination and reduced exposure time for black-and-white and color photography but was considered too cumbersome for practical application at that time

In 1951, a group working at the National Scientific Research Institute in Paris[7] devised a bronchoscope which was illuminated by means of an exterior light source transmitted through a quartz rod Color pictures were reported to have been taken through these instruments In 1955 Dr Jaupitre[8] reported color

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[7] Drs Fourestier and Gladu and Mr Vulmiere, French patent No 1,036,992

[8] Doctor Michel Jaupitre, August 4, 1956, Revue du Film Medical et Chirurgical, Supple to Semaine des Medical, No 46–47, August 4, 1956

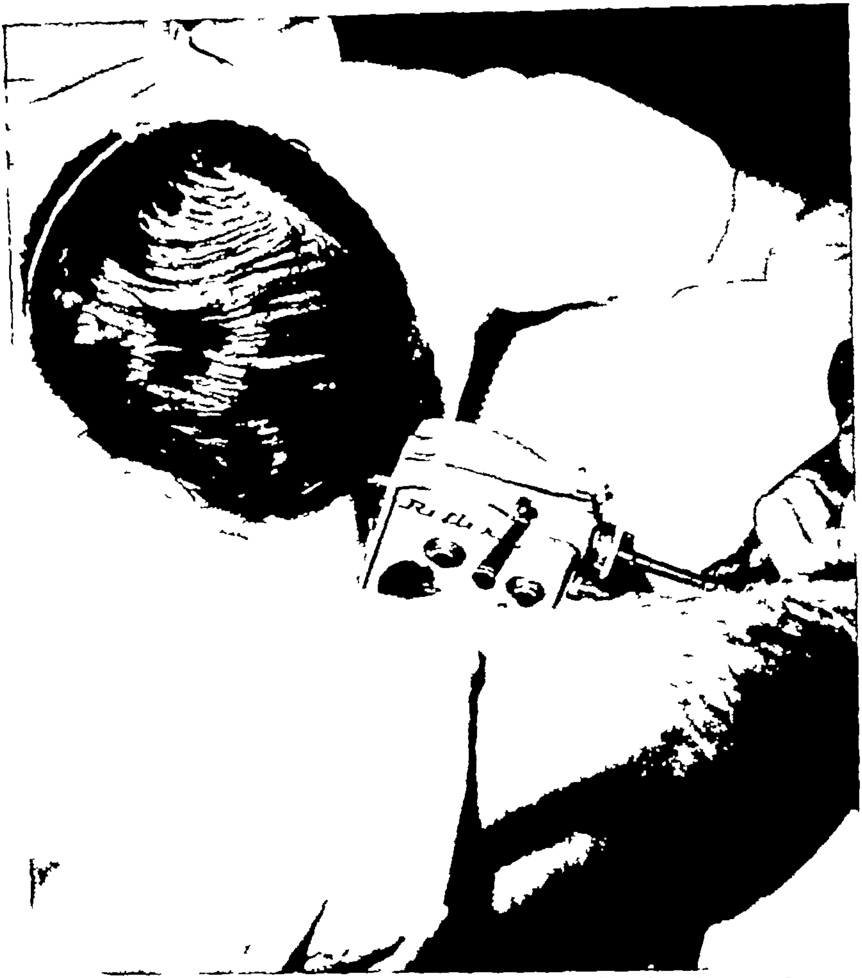

FIG 3 Illustrates reflex motion picture camera in bladder photography

photography through an air endoscope utilizing an exterior light source and quartz rod illumination Fay[9] and others[10] reported color films and transvesical views

The quartz rod panendoscope which we are about to describe is the culmination of work begun in 1947 previously described This instrument has been used very successfully in televising the interior of the human bladder It marks a great advance in the visualization of the bladder and provides a superior means for teaching medical students various urological procedures The instrument consists of a standard McCarthy panendoscope sheath, with a cone offset to accommodate the accessory light transmitting source The optical system consists of an en-

[9] Fay 1955 Color films transvesical views Societé Médicale pour l'Étude Photocinematographique Endoscopique

[10] Michon color film air medium urethroscopy Societé Française d Urologie, June 1955

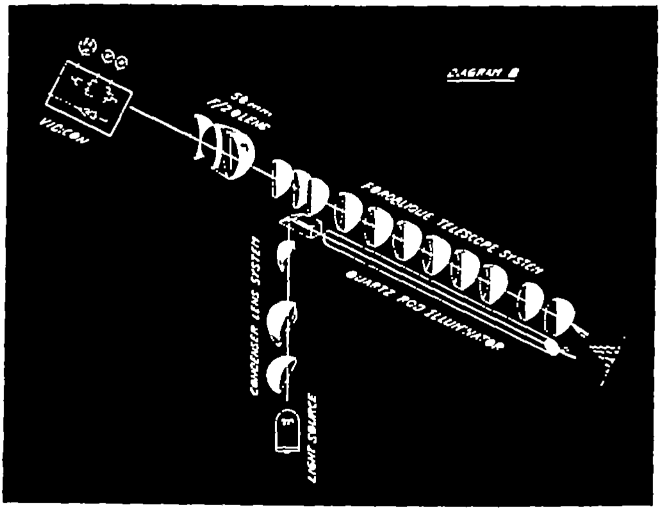

FIG 4 Optical system using television

larged version of the McCarthy foroblique telescope The telescope is attached to a cylindrical container which serves as a means for mounting the telescope and for retaining the optical condensing system which collects the light and transmits it to the quartz light conducting tube This system is illustrated schematically (fig 1) A 50 or 100 watt incandescent 8 volt light bulb having a prefocused filament is attached to a socket and a flexible cable which provides voltage sufficient to illuminate the lamp, and enough circulating air to keep the lamp cool The air is diffused by means of baffles in the cylindrical container A low pressure centrifugal air supply system is located in an accessory case which contains indicator lamp, rheostat for regulation of voltage, isolation transformer for power source and a footswitch for overloading lamp voltage if desired The light transmitted through this system is sufficient to provide illumination adequate to take color still pictures at exposures of $\frac{1}{25}$ second at a working distance of $\frac{3}{4}$ inch For still colored pictures the reflex Kine Exacta fitted with suitable adapter, or the Praktina FX, F2 lens has been used successfully For color motion pictures a speed of 16 frames per second is possible (figs 2 and 3) Black-and-white television is practicable with the illumination provided

In the television system the camera containing the image tube is coupled to the ocular end of the foroblique telescope The optical image is converted electronically in the image tube of the camera and transmitted to a cathode ray television viewing screen (fig 4) An operator views the interior of the bladder by observing the television screen (fig 5) As many observers as can be accommodated in a room can view the television screen If desired, other television viewing screens can be located in amphitheatres, or at some distance from the cystoscopic room, and may be viewed simultaneously Future advances in transistorized television camera optical image tubes and accessory equipment hold out the possibility for large scale color television of the interior of the bladder

Color motion pictures of the interior of the bladder have been taken, utilizing an 8 mm reflex motion picture camera of the Camex type or 16 mm reflex of the Bolex type The same telescopes and illumination systems are used with the motion picture camera as utilized with the television arrangement The ocular of the telescope is attached to a 12 5 mm Fl 9 lens and the entire system attached to the reflex camera by means of a bayonet lock The camera is operated at speeds of 8 or 16 frames per second, depending on the working distance and conditions to be observed The light intensity provided by the foroblique quartz panendoscope is more than adequate to fulfill the light requirements of the color

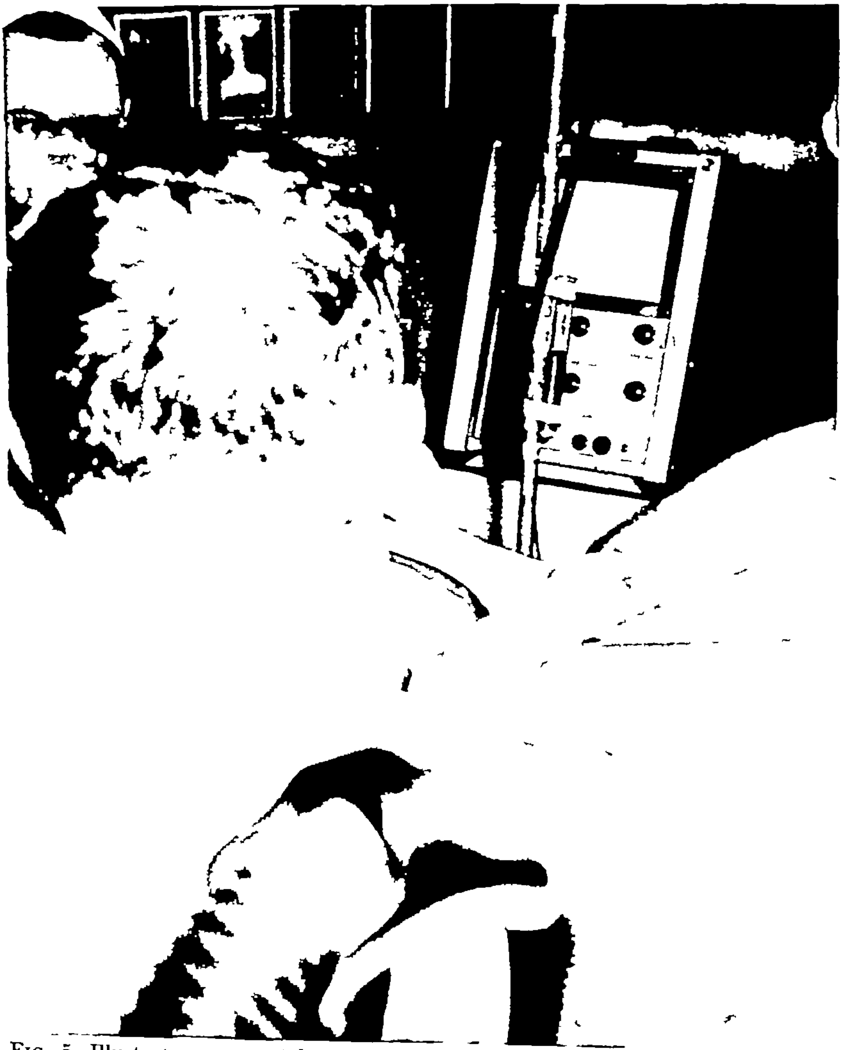

FIG 5 Illustrates camera televising interior of bladder Note position of television screen to operator

films Illumination is adequate and color values are faithfully reproduced This system provides means of obtaining motion pictures of benign and pathological bladder conditions and operative urological procedures Films of this type should provide a very useful addition to our teaching armamentarium and should be useful for documentation

Television is the more spectacular of the two procedures just described but it will require many adjustments, some of which are now in the process of formulation Colored motion pictures seem to the authors to be ready for immediate application The demonstrations were conducted successfully by Dr J Sydney Ritter

This investigation called for so many skills, scientific and clinical, that it has been difficult to assign credit to everyone involved The project as a whole was sharply divided between the scientist and clinician The credit for the inception of the plan, the optical, photographic, and electronic aspects, must go to the scientists of the American Cystoscope Makers, Inc , under the leadership of Mr Frederick J Wallace, to whom the authors wish to express their appreciation

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VAGINAL DIAPHRAGM CATHETERS

HERBERT D. WOLFF, JR. AND NORMAN A. GILILLAND

Urinary leakage from ureterovaginal or vesicovaginal fistula can be controlled in many instances by the use of a properly fitted vaginal diaphragm to which a mushroom catheter with drainage receptacle has been attached. Patients can be comfortable while working at their usual occupations for periods of four to six months in preparation for corrective surgery.

The terminal two-thirds of the head of an ordinary mushroom catheter is removed, leaving a straight tube with a right angle flange. A small hole (3 mm.) is then cut in the rubber diaphragm at what will be the most dependent spot when worn by the patient. The drain tube of the amputated mushroom catheter is pulled through and the residual catheter head is attached with rubber glove cement.

We hope that the edges of the vaginal diaphragm in the future will be better padded because by constant usage they can produce ulcerated areas in the vagina. Hence the patient is instructed to change the diaphragm catheter frequently, leaving it out every third to fourth night or when convenient. This is particularly true in cases of malignant involvement or those that follow radiation therapy. In such individuals the vagina is generally contracted and the local tissues have a circulatory deficiency so that the rim edge of the usual diaphragm (fig. 1 *A*) may ulcerate into the vaginal wall. In these cases it is better to use the smaller cervical cup catheter (fig. 1 *B*) with its larger, softer, rounded edge and let the patient wear this for daytime or partial use. Unfortunately, the cervical cup diaphragms are not available in the larger calibrated sizes. Experience has shown that measures to decrease precipitation of urinary salts are wise during the use of such vaginal diaphragm catheters.

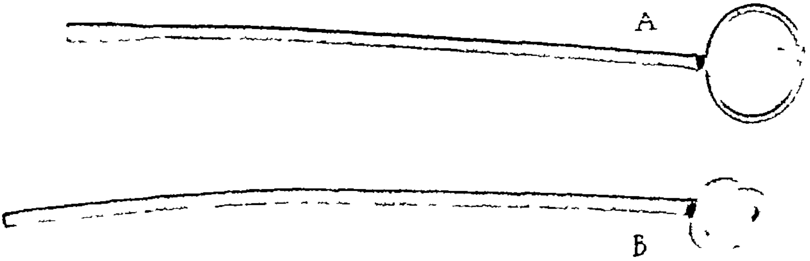

FIG. 1. *A*, vaginal diaphragm catheter. *B*, cervical cup catheter.

Both C. R. Bard Inc. and American Cystoscope Makers Inc. will furnish such diaphragm catheters, ordered by size after careful fitting by the physician with the usual vaginal rings. These last much longer than the homemade variety described and shown in figure 1 which, however, can be easily made for temporary use while awaiting delivery (approximately four to six weeks).

706 Duke St., Alexandria, Va.

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USE OF SEGMENTS OF SMALL AND LARGE INTESTINE IN UROLOGICAL SURGERY, WITH SPECIAL REFERENCE TO PROBLEM OF URETEROCOLIC ANASTOMOSIS

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Mr. President, I wish to thank you and the American Urological Association for the great honor you have done to me and to British urology in inviting me to give the Ramon Guiteras Lecture. The first Guiteras lecturer in 1929 was the late Professor A. von Lichtenberg of Berlin, a distinguished urologist whose clinical assistant it was my privilege to be for some months in 1933 to 1934.

Dr. Guiteras, a man of very great energy and achievement in many spheres including athletics, field-sports and travel, devoted most of his active surgical life to the practice and study of genitourinary surgery. His first important appointment, as became a pioneer in a special field, was as professor of anatomy and operative surgery in 1893; later he became professor of genitourinary surgery in the New York Post-Graduate Medical School. Doubtless at that time he saw the inevitability of specialization in a narrower field of surgical achievement and when the opportunity came he embraced it. It is perhaps appropriate that much of what I shall describe today concerns the surgical borderland between general surgery and urology.

PRELIMINARY CONSIDERATIONS

Isolated segments of the large and of the small intestine have been used in my department by my colleague, Mr. F. P. Raper, and myself for incorporation into the urinary tract in 72 operations in 69 patients.

The operations are of two kinds. In one group, in which loops of ileum are used, the operation aims at the remodeling of part of the urinary tract (the ureter or a portion of the bladder) so as to restore it anatomically to serve its original purpose. In the second group, in which loops of the small *and* of the large intestine are used, the operation aims at constructing a conduit or a reservoir for urine, as a method of urinary diversion alternative to the orthodox ureterocolic anastomosis. The muscular coats and the mucous membranes of both the small and the large intestine have physiological properties which differ from those parts of the ureter and of the urinary bladder which they are to replace and may modify the purely anatomical results of these procedures, though the overall advantages can be very great.

Large intestine. When an isolated segment of the rectosigmoid colon or of the ileocecal region is used to constitute an artificial bladder, there is little risk of interference with their blood supply and the loops remain fixed in their natural sites in the abdominal cavity. It has been shown by various workers, however, that the mucous membrane of the colon readily absorbs electrolytes from the

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Ramon Guiteras Lecture presented at annual meeting of American Urological Association, Pittsburgh, Pa., May 6–9, 1957.

TABLE 1 *Uses of segments of the small and large intestine, 72 operations*

A Remodeling operations (using a loop of ileum)			
1 To replace a part of the ureter		4	
2 Ileocystoplasty			
i) To enlarge a contracted bladder	15		
ii) To reanastomose ureters to the bladder	3	18	
3 To reconstruct a bladder after complete removal (ileourethral anastomosis)		3	25
B For urinary diversion			
1 Rectosigmoid bladder		20	
2 Ileal bladder (ileal segment or ileal ureterostomy)		27	
3 Ileocecal bladder			47
			72

urine, chloride ions being absorbed in excess of sodium ions (Ferris and Odel, 1950, Lapides 1951, Parsons, Pyrah, Powell, Reed and Spiers, 1952, Parsons, Powell and Pyrah, 1952) A new point has recently emerged

It has usually been assumed that this differential reabsorption of electrolytes from the colon remains for an indefinite period quantitatively the same We have recently examined the extent of the reabsorption of these two ions from the isolated rectosigmoid in two cases, eight and 22 months respectively after the first test, and we have found that the amount of chloride ions absorbed had then approximated much more closely to that of the sodium ions, the change being greater for the greater time interval This finding, which suggests that there may have been some adjustment or adaptation of the colonic mucous membrane, was shown in the following way

In two patients, each having equally functioning kidneys, who had had the left ureter transplanted into an isolated rectosigmoid bladder (fig 1, *A*), a known amount of bladder urine containing tracer amounts of radioactive chlorine (chlorine ^{38}) and sodium (sodium^{24}), was instilled into the rectum after the latter had been completely evacuated During the period of retention of the enemas, samples of blood were withdrawn at intervals and their radioactive concentrations of chlorine^{38} and sodium^{24} were measured, the analysis depending on the difference in decay rates of the two isotopes Allowance was made for the different effective spaces and rates of movement into them, of the sodium and chloride ions (Reed and Care, 1954) and also for the effect of isotopic dilution during the course of the experiment After a period of retention which varied between 70 and 108 minutes, the rectal bladder was emptied completely Samples of both introduced and returned fluids were analyzed chemically and also for radioactivity In this way the loss of chloride and of sodium ions from the enema urine, and their appearance in the bloodstream could be expressed in terms of milliequivalents The investigations were repeated in the same patients 22 months and 8 months later respectively, cystectomy and transplantation of the remaining ureter into the rectosigmoid bladder having been carried out after the first investigation (fig 1, *B*)

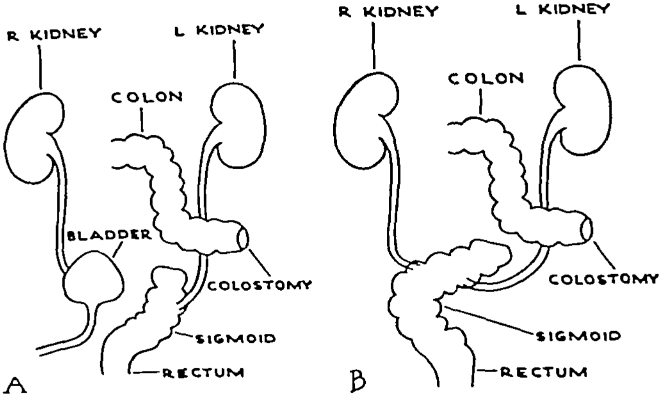
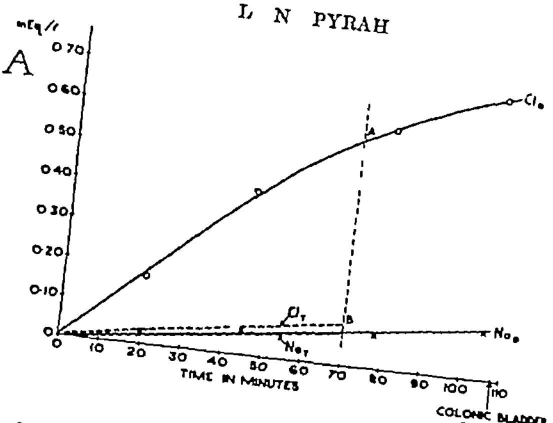


FIG 1 Diagram of rectosigmoid bladder *A* sigmoid divided, left ureter attached to new ‘bladder’, colostomy established *B* bladder has been removed, right ureter has been attached to new ‘bladder’

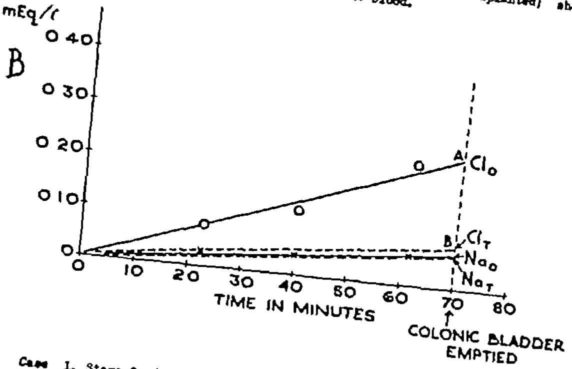
The results obtained from the movement of sodium and chloride ions across the colonic mucosa into the blood in one of these cases are shown in figure 2 The continuous lines Na_0 and Cl_0 represent the observed uptakes by the blood, of sodium and chloride ions The dotted lines Na_T and Cl_T, show the relative concentrations to be expected if the sodium and chloride ions had been absorbed in equivalent amounts The ratio of the ordinates A and B at the selected time 70 minutes, may be used as a measure of the differential uptake of chloride ions relative to sodium ions The closer this ratio is to unity, the more nearly are the chloride and sodium ions absorbed in equivalent amounts Figure 2, *B* shows the marked reduction of the excess of chloride ions relative to sodium ions as indicated by the distance AB, which occurred when the experiment was repeated after 22 months Similar findings were recorded in the second patient examined eight months after cystectomy (Care, Reed and Pyrah, 1957)

This result, which we have demonstrated in the isolated rectosigmoid colon may well apply to the intact colon, and it is in accord with the clinical observation that the health of many patients with ureterocolic anastomosis becomes more stable, possibly with a diminished tendency to acidosis, some months after the operation, provided renal function be not greatly impaired (Priestley 1949, Rosenberg 1953)

Ileum Turning now to the small intestine, an isolated loop of the lower ileum is convenient anatomically for incorporation into the urinary tract The lower end of the selected loop should be some inches from the ileocecal valve while the upper end must be at an appropriately high level in accordance with the use for which it is designed The transverse vascular arcades are divided between ligatures at the two proposed places of section of the gut, making two oval openings in the mesentery, the vitality of the gut is not endangered unless the pedicle of the loop is too narrow, when rotation could cut off the blood supply to the loop and cause gangrene The gut is crushed in a crushing clamp and divided, leaving the metal guards or clamps temporarily in position, or closing the two ends, according to the use to which the loop is to be put Continuity of



Case 1. Stage 1. The absorption of Na^{24} and Cl^{38} ions from an isolated portion of distal colon (to which one ureter has been transplanted) shown by the appearance of radio-activity in the blood.



Case 1. Stage 2. (22 months later) The absorption of Na^{24} and Cl^{38} ions from an isolated portion of distal colon (to which both ureters have been transplanted) shown by the appearance of radio-activity in the blood.

FIG 2 By courtesy of Clinical Science (vol 16, p 95, 1957)

the intestine is restored by end-to-end or lateral anastomosis, usually in front of the mesentery of the loop, the opening between it and the anastomosis being closed by interrupted sutures The loop is sufficiently mobile to be brought into either iliac fossa or into the pelvis without tension and its muscular wall still retains the power of active peristaltic movement

Before using the ileum extensively for incorporation in the urinary tract, it was important to see if electrolyte absorption was likely to give rise to clinical symptoms In a patient who had an *excluded, intact bladder* (who will be referred to later) it was shown by perfusion experiments using the radioisotopes ^{24}Na and ^{38}Cl, that sodium and chloride ions migrate across the epithelium of such an excluded bladder into the blood, and also in the reverse direction from the blood into the experimental fluid within the bladder, in approximately equivalent amounts When the bladder was enlarged by anastomosing a loop of ileum to it, it was shown that there was a small net absorption of chloride and of sodium ions in almost equivalent amounts and therefore there should be no hyperchloremic acidosis (Pyrah, Care, Reed and Parsons, 1955)

In another case, a woman with polycystic kidneys and renal failure, in which an attempt was made to utilize a four-foot isolated loop of ileum as an auxiliary kidney by irrigating it with various fluids, in order to reduce the blood urea and restore the blood electrolytes to normal, we were able to perfuse the loop with various ion-containing fluids in order to study their migration (Pyrah and Care, 1957) Potassium ions were shown to move simultaneously in both directions across the ileal wall, when the potassium concentration in the perfusing fluid was approximately three times that in the plasma (the cellular potassium being normal) there was a net movement of potassium from the loop into the blood which could result in hyperkalemia Since the potassium concentration in the perfusion fluid at which absorption of potassium into the bloodstream occurred, was generally about one-half of the potassium concentration of average urine, it seemed highly probable that absorption of potassium into the bloodstream would take place when ileum was incorporated into the urinary tract If the renal function was normal, homeostasis of the potassium could be achieved, but if it was impaired there would be danger of hyperkalemia (Pyrah, Care, Reed and Parsons, 1955)

In the dog, Tasker (1953) showed that absorption of potassium takes place from a bladder enlarged by a loop of ileum, he also reported a case of ileocystoplasty, in which death from hyperkalemia was suspected as a result of absorption of potassium, and the subsequent failure in the mechanism of it excretion because of oliguria

It seems, therefore, that a loop of ileum can be incorporated into the urinary tract with little fear of hyperchloremic acidosis but that hyperkalemia may occur if renal function is inadequate

ILEAL LOOP USED TO REPLACE A PART OR THE WHOLE OF THE URETER

Some tumors of the ureter and also certain injuries, strictures or fistulas, may be treated by excision of part or the whole of the ureter and replacement by a loop of ileum, instead of performing nephro-ureterectomy

For small, localized tumors of the *lower end* of the ureter, and for limited injuries of its terminal part during gynecological procedures, reimplantation of the divided ureter into the intact bladder or into a long tubular flap of the whole thickness of the bladder wall, after the method of Boari (1896), will usually suffice The replacement of a portion of the ureter by a loop of ileum can be used in cases in which a part of the ureter has been injured over a considerable length, or in which the removal of the tumor together with possible seedlet tumors below it necessitates the excision of a longish portion of the ureter, from a site above the level of the tumor down to and including the ureteric orifice in the bladder It is necessary to be as certain as possible by means of pyelography that the case is one of a *primary* ureteric tumor and that the renal pelvis and calyces are tumor-free

Previously recorded cases A loop of ileum was first used to replace a part of the ureter by Nissen (1940) Longuet (1948) reported a similar operation for an injury to a ureter during Wertheim's operation for uterine cancer while Muller (1950) joined both ureters, which had been injured during a Wertheim's operation, to the ends of an isolated ileal loop, which was then anastomosed to the bladder Foret and Heusghem (1953) in a patient with bilateral narrowings of the ureteric orifices, joined the divided ends of the ureters to the limbs of a U-shaped ileal loop, the center of which was anastomosed to the bladder Baum (1954) replaced a part or the whole of the ureter in three cases of fibrous ureteric stricture, and also in a fourth case with ureteric obstruction resulting from a malignant metastasis Ortved (1954) used a similar technique to replace the lower half of a ureter previously damaged by manipulation for the removal of stone Fergusson (1956) reported a case of massive left hydronephrosis, the right kidney being almost nonfunctioning, for which a left nephrostomy had been done as a life-saving measure, in an attempt to relieve the ureteric obstruction responsible for the hydronephrosis, an isolated ileal loop was interposed between the enlarged renal pelvis and the bladder It was found, however, that when the urethral catheter was withdrawn, very little urine was passed per urethram, while the nephrostomy continued to drain, evidently because the ileal loop and the huge distensible hydronephrotic sac to which it was joined, offered less resistance to the flow of urine than that offered by the bladder sphincters and the urethra Nephrostomy drainage was therefore continued

Wells (1956) collected a series of 24 cases in which part of the ureter had been replaced by ileum, the series included 10 cases of ureteric damage or involvement, five of ureteric tumor, five of ureterovaginal fistula and four of mega-ureter

The operation The lower half of the ureter is most easily reached extraperitoneally through a paramedian incision ending below at the pubic symphysis, a long oblique incision in the line of the ureter, ending near the pubis, may be more suitable for excising the lower two-thirds of the ureter together with a circle of bladder wall, for tumors in the middle third The ileal loop may be placed either *extraperitoneally* by being brought into the line of the excised ureter through an opening in the lateral wall of the parietal peritoneum, or it may be placed *inside* the peritoneal cavity, when it is sutured to the parietal peritoneum by interrupted stitches (fig 3) When the ileum replaces the lower part of the *right* ureter, the urine draining into the bladder has to flow against the peristaltic contractions of the ileum but no disadvantage seems to follow, when the loop replaces the lower part of the *left* ureter, the urinary flow is isoperistaltic

We have treated three patients with primary ureteric tumors and one patient with injury of the ureter, by excision of a part of the ureter and replacement by ileum

Case 1 Figure 4, *A* shows the intravenous pyelograms of a man aged 52 who had had three attacks of hematuria with left renal pain, he had left hydronephrosis of calyceal type and a filling defect in the lower third of the ureter indicative of tumor (fig 4, *B*) This patient was treated by extraperitoneal excision of the lower third of the ureter together with a circle of bladder wall containing the ureteric orifice, the excised ureter was replaced by a loop of ileum, which was allowed to prolapse through an opening in the lateral parietal peritoneum and was then sutured in front and behind to the ileal loop The hydronephrosis improved considerably (fig 4, *C*) A cystogram showed no ureteric reflux though

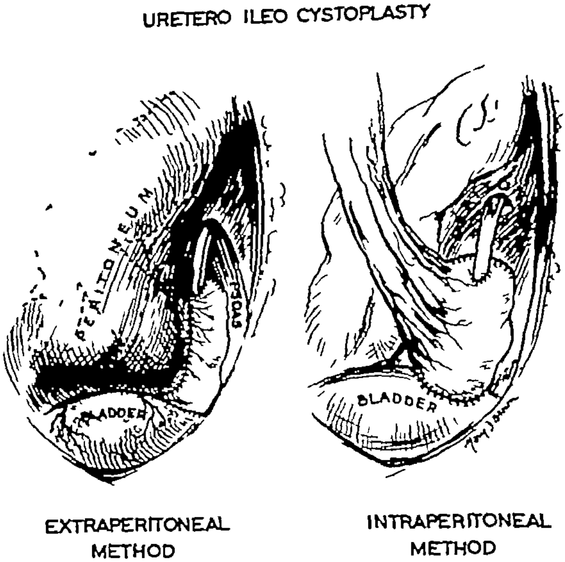


FIG 3 Diagrammatic representation of replacement of excised lower third of ureter (ureteroileocystoplasty) by coil of small intestine, in extraperitoneal method coil of ileum prolapses through opening in lateral peritoneum, to edges of which it is stitched, in intraperitoneal method isolated loop of ileum is sutured to peritoneum of iliac fossa

the ileal loop was well filled (fig 4, *D*) Perfect healing occurred between the ileal and the vesical mucous membranes This patient, who had an anaplastic growth of the ureter, died 15 months after operation from metastases in the posterior part of the abdomen

Case 2 A woman aged 46 had an extensive endometrial tumor (fig 5, *A*), undiagnosed by preliminary biopsy, involving the vaginal vault, the cervix of the uterus, the base of the bladder and the left ureter (resulting in pyonephrosis) I treated this case by removing the upper half of the vagina and the uterus, the left kidney and ureter and the base of the bladder The right ureter, which was intimately connected with the mass, was damaged at operation and was reimplanted into the reconstructed bladder The anastomosis proved unsatisfactory and ureterostomy was done on the third postoperative day Later, continuity of ureter and bladder was restored by a loop of ileum replacing the damaged ureter This patient remains well Figure 5, *C* shows a recent radiograph of the renal tract with the ileal loop in situ, slight hydronephrosis is present

The late results of ileal replacement of the ureter cannot be assessed on a basis of a small number of cases though the early results have been satisfactory, there is, of course, a possibility of the occurrence of late intestinal obstruction because of adhesions in such cases

ILEOCYSTOPLASTY

Isolated loops of ileum have been used to enlarge a small bladder

Previous cases Ileocystoplasty was first done by von Mikulicz (1898) Shoe-

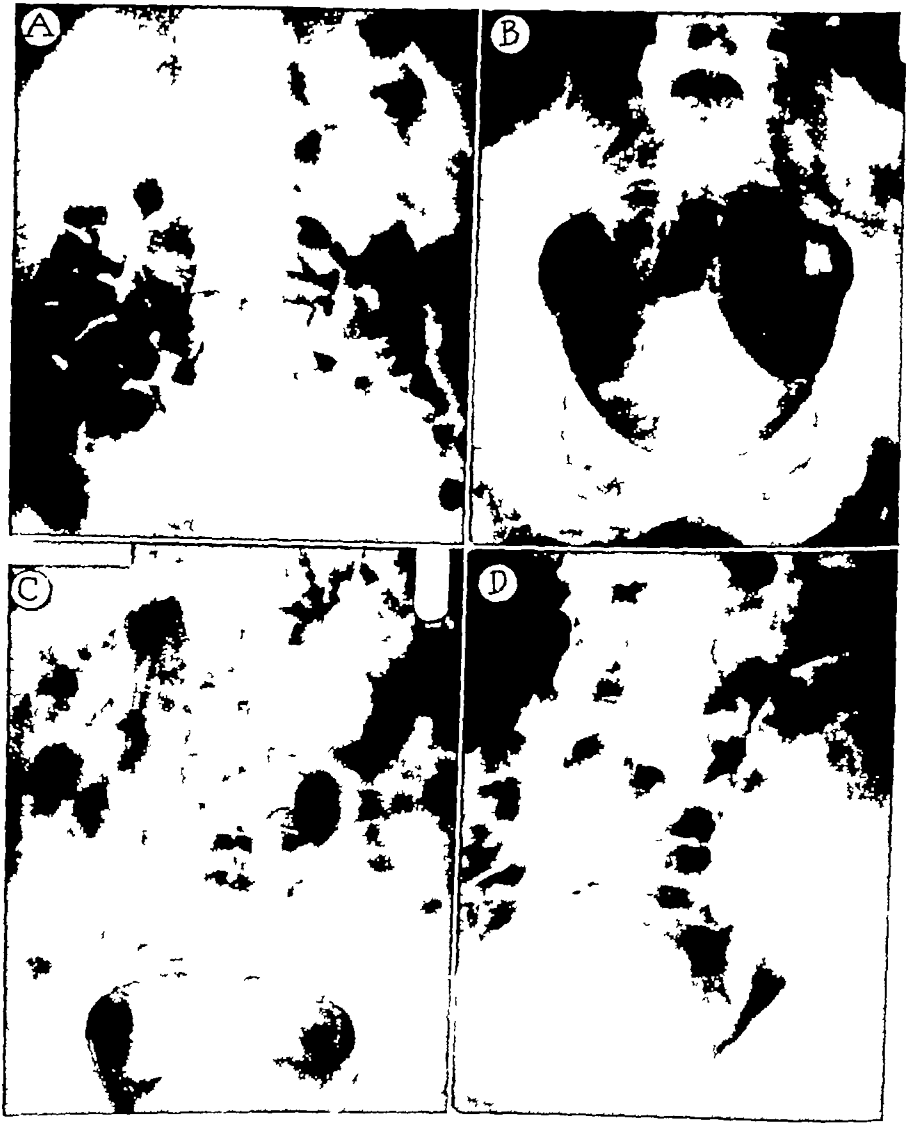


FIG 4 Case 1 Primary carcinoma in lower third of ureter *A*, medium grade left hydronephrosis *B*, filling defect in lower third of left ureter *C*, postoperative intravenous pyelogram shows some reduction in hydronephrosis after ureteroileocystoplasty *D*, postoperative cystogram shows reflux from bladder up ileal loop, no reflux up residual part of ureter (By courtesy of British Journal of Surgery vol 42, p 357, 1955)

maker (1909) carried out the operation in two stages for a contracted bladder which was probably tuberculous, in the first stage the sole remaining ureter was implanted into an ileal loop which was brought out through an opening in the abdominal wall, later the loop was anastomosed to the bladder In the next 30 years the European literature records a number of single cases of the operation, sometimes the center of the ileal loop was joined to the bladder, the ends being closed, sometimes one end was closed, the other end being anastomosed to the

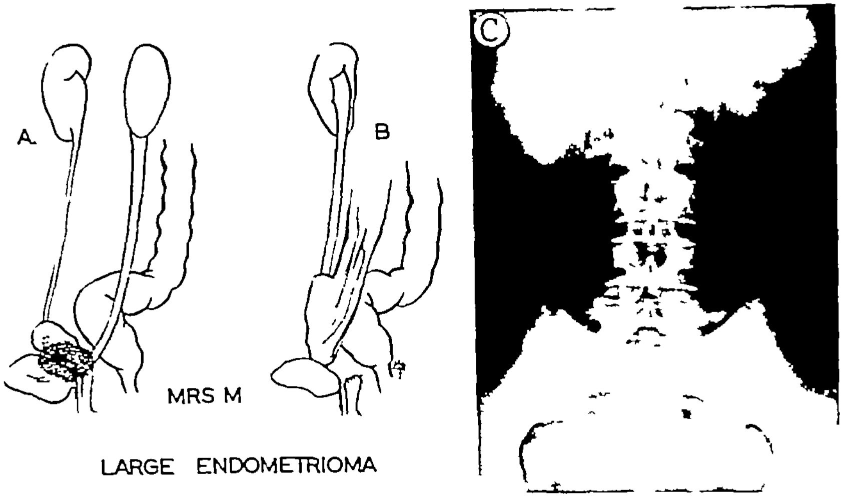


Fig 5 Case 2 Mrs M aged 46 *A & B*, diagram shows location of large endometrial tumor involving vaginal vault cervix uteri, bladder and left ureter For description, see text *C*, postoperative pyelogram of right kidney and ureter lower half of ureter has been replaced by ileum, slight hydronephrosis

bladder Similar operations to enlarge the bladder, referred to elsewhere (Pyrah and Raper, 1955), were also done using short segments of the sigmoid colon or of the cecum Scheele (1941) anastomosed the center of an isolated loop to the bladder and joined the ends of the loop together, producing a ring of ileum joined to the dome of the bladder Interest in these procedures was revived by Couvelaire (1950) who described 5 cases in which he had enlarged a small, healed, tuberculous bladder by joining to it an isolated loop of cecum (3 cases) or of ileum (2 cases), in the last two cases the dilated ureters of the sole remaining hydronephrotic kidney were joined to the ileal loop and the patients were relieved of their frequency Cibert and his co-workers (Cibert 1953, Cibert, Durand, Foret and Soler, 1954, Cibert and associates, 1955) have now reported 60 cases of ileocystoplasty for healed, contracted, tuberculous bladder

Present series A closed, isolated loop of ileum has been anastomosed to the bladder for the various purposes shown in table 2 in 18 cases, the indications have been to enlarge a contracted bladder resulting from long-standing chronic cystitis, from healed tuberculosis or from interstitial cystitis, to reconstruct a bladder after a large part of it has been excised surgically, to correct the frequency resulting from an uninhibited bladder, and to effect a *restitutio ad integrum* following ureterocolic anastomosis in cases in which the bladder is still present The three cases in the last group are revision procedures and will be referred to later

Pathology Fibrous contracture of the bladder following long-standing cystitis or healed tuberculosis may reduce its capacity to three, four or five ounces resulting in intolerable day and night frequency

The healed tuberculous bladder, scarred and subdivided by prominent septa and wide saccules, may be reduced to extremely small proportions and in such

TABLE 2 *Ileocystoplasty using a closed ileal loop*

	Cases	Deaths
A For a contracted bladder		
1 *Long standing chronic cystitis ileocystoplasty*	1	
2 Healed, contracted, tuberculous bladder		
a Ileocystoplasty	5	1
b Ureteroileocystoplasty	3	1
3 Interstitial cystitis ileocystoplasty	4	
B To reconstruct the bladder after extensive partial cystectomy	1	
C For uninhibited bladder	1	
D To effect a *restitutio ad integrum* following ureterocolic anastomosis (bladder still present)		
Unilateral or bilateral ureteroileocystoplasty	3	
	18	2

cases the detrusor muscle may have undergone destructive atrophy, though the trigone does not seem to contract and may even appear to be larger than normal The ureter of the other kidney may remain normal or it may be dilated from spastic contracture of its lower end or from a mucosal stricture of its terminal part, or the ureteric sphincter may become incompetent, resulting in reflux In the smallest bladders the prostatic urethra undergoes a remarkable degree of dilatation which can be seen on urethroscopy, the bladder neck being wide open, the gaping openings of the dilated prostatic ducts can easily be seen A cysto-urethrogram shows that the prostatic ducts are changed into bulbous, dilated pockets in the substance of the prostate Even the stump of the ureter of the excised kidney has here taken part in the dilatation, as if to provide every scrap of room for the storage of urine There may be reflux up the remaining ureter The external sphincter remains intact except in the more advanced cases With the atrophy of the detrusor muscle, the vesical opening of the remaining ureter appears to become displaced to the posterosuperior angle or corner of the small bladder It is such small distorted bladders with their still undamaged external sphincters that ileocystoplasty is designed to relieve

The operation In most of the cases in our series the center of the ileal loop has been anastomosed to the posterior wall or the dome of the bladder (figs 6 and 7) The length of the loop varies in inverse proportion to the size of the bladder to be remodeled For a very tiny "thimble" bladder a loop 12 or 15 inches in length has been used, shorter lengths being employed for a bladder with a capacity of 4 to 6 ounces After the loop has been prepared in the case of the four-ounce bladder, the peritoneum over the posterior wall of the bladder is incised transversely a little distance below the vault and is dissected up and down so as to expose a suitable part of the muscular wall When the bladder is very tiny, and the detrusor muscle is atrophied, it is best to excise the fibrosed detrusor muscle, as recommended by Cibert (1955), care being taken not to injure the remaining ureter because of its abnormal position The anastomosis is made by two rows of continuous catgut sutures, the outer layer being between the sero-

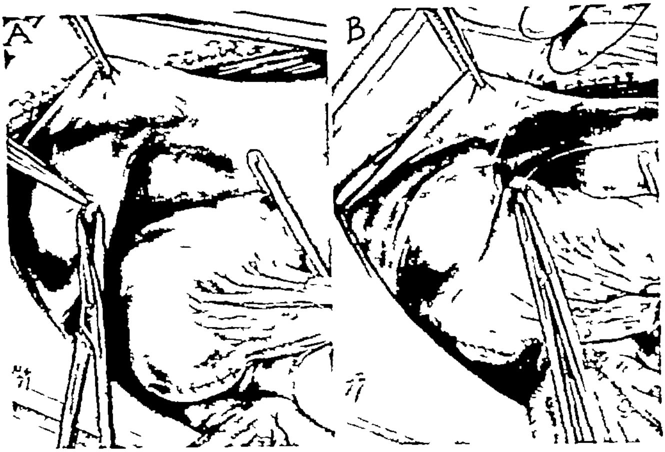


FIG 6 Operation of ileocystoplasty A, ileal loop has been isolated, proximal end has been infolded, clamp remains on distal end for implantation of ureter B, ileal loop is stitched by continuous suture to back of bladder

muscular layer of the intestine and the outer part of the muscle coat of the bladder, and the inner layer being through the whole thickness of the wall of the intestine and the deeper muscle layer and the mucosa of the bladder, bringing the two mucous membranes into accurate apposition The peritoneum previously reflected from the bladder wall is sutured to the intestine in such a way as to make the anastomosis itself extraperitoneal The abdomen is closed but a drain is left in the cave of Retzius A catheter remains in the urethra 10 days

If there is no hydronephrosis of the sole remaining kidney, a simple ileocystoplasty is done if the kidney is hydronephrotic from ureteric stricture, the ureter should be mobilized, divided and implanted into the end of the ileal loop, when improvement in the hydronephrosis can be gradually expected (fig 8) If the hydronephrosis is the result of ureteric reflux, some surgeons have found improvement of the hydronephrosis by a simple ileocystoplasty, the ureter not being reimplanted, my own preference so far has been to reimplant the ureter into the loop in such cases

Case 3 A man of 31 had had a left nephro-ureterectomy for tuberculous kidney in May 1950 The bladder two years later had undergone contracture and early dilatation of the right kidney and ureter was present By 1953 frequency of micturition had increased to half-hourly by day and five to six times at night, sometimes with nocturnal incontinence, the urine was pus- and tubercle-free, intravenous pyelograms now showed an increase in the hydronephrosis and hydroureter (fig 9, A) On cystoscopy, the capacity of the bladder was 3 ounces but the mucous membrane was completely healed Ureteroileocystoplasty was done on May 27, 1953, the ureter being placed into the distal end of the ileal loop A recent intravenous pyelogram (fig 9, B) shows that the hydronephrotic kidney has returned to normal Micturition is normal by day and he does not micturate during the night The urine is sterile

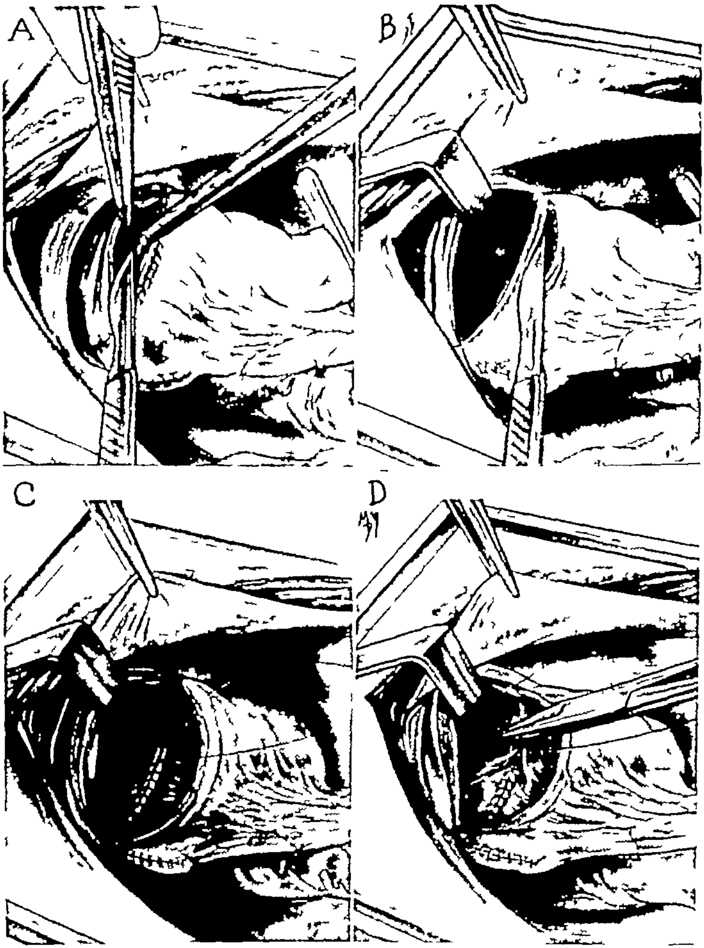


FIG 7 Operation of ileocystoplasty *A*, opening is made into cavity of bladder *B*, opening of same size is made into lumen of intestine *C*, continuous suture approximates mucosae of ileum and bladder *D*, last suture line is continued

Two operative deaths have occurred among the 17 cases, testifying to the magnitude of the procedure One patient died from ileus due to intestinal obstruction, the other died from renal failure, the sole remaining kidney being hydronephrotic

Results The late *clinical* results of these procedures are usually excellent The intolerable frequency of micturition has been relieved in nearly all cases, giving sleep at night and improved general health These people are among our most grateful patients In only two has frequency persisted and both have residual urine The operation of ureteroileocystoplasty for a small, healed, tuberculous bladder with hydronephrosis of the remaining, otherwise healthy, kidney, promises to offer protection to the kidney and to be a considerable advance over ureterocolic anastomosis, in such cases

The late *mechanical* results in the bladder itself have been studied by retro-

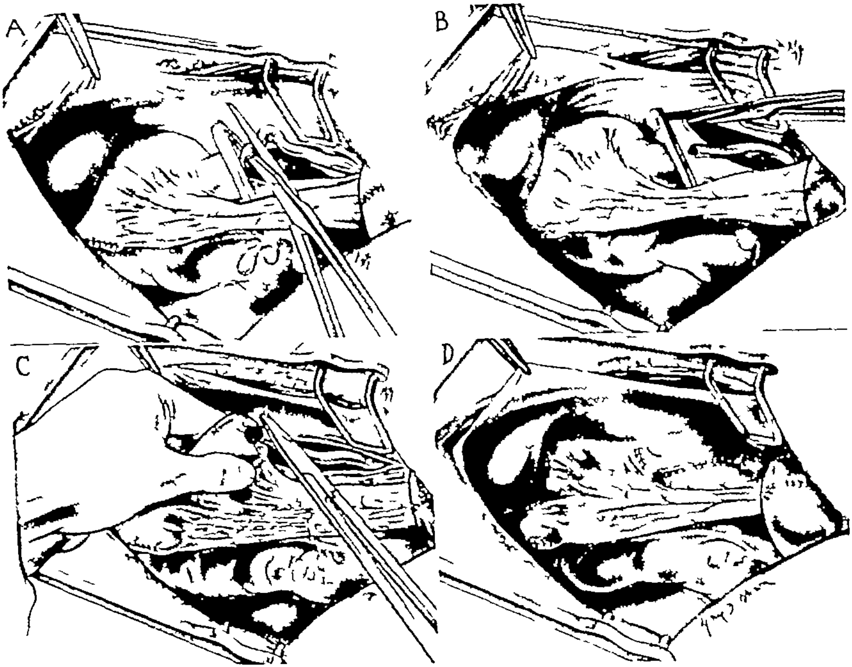


Fig 8 Operation of ureteroileocystoplasty *A*, right ureter mobilized after incising peritoneum *B*, ureter divided *C*, suitable technique for anastomosing stump of divided ureter to end of ileal loop, outermost parts of end of ileum are sutured and infolded, ureter is joined by mucosa-to mucosa anastomosis to middle of divided end of loop *D*, completed operation

grade cystograms and by estimations of the residual urine Hanley (1956) has also made studies with the image intensifier When opaque medium is injected into the bladder by catheter, the loop fills quite well (fig 10, *A*), serial radiographs taken at a few seconds interval demonstrate that the ileum retains its peristaltic activity, as in the case shown in fig 10, *B*, which shows different phases of relaxation and contraction of the ileal loop In a small number of cases the ileal loop has remained inactive during the period of the examination When micturition commences, the medium is partly expelled per urethram and partly into the loop which is then stimulated to contract and empty, the act of micturition is then biphasic and may take longer than a normal act, and may have to be assisted at first by gentle manual pressure over the abdomen

After micturition, in some cases the bladder and the loop empty completely as in the case shown in figure 11, here the operation was for a three-ounce healed tuberculous bladder, the upper tract remains normal, no reflux developing Figure 12 shows the cystogram of a case with a very small residual urine, in a man with ureteroileocystoplasty done four years ago, the clinical result is excellent Most of our cases are like this In a small minority there is a moderate amount of residual urine In one such case cystography shows the bladder and the loop filled (fig 13, *A*), after voluntary evacuation the bladder proper and

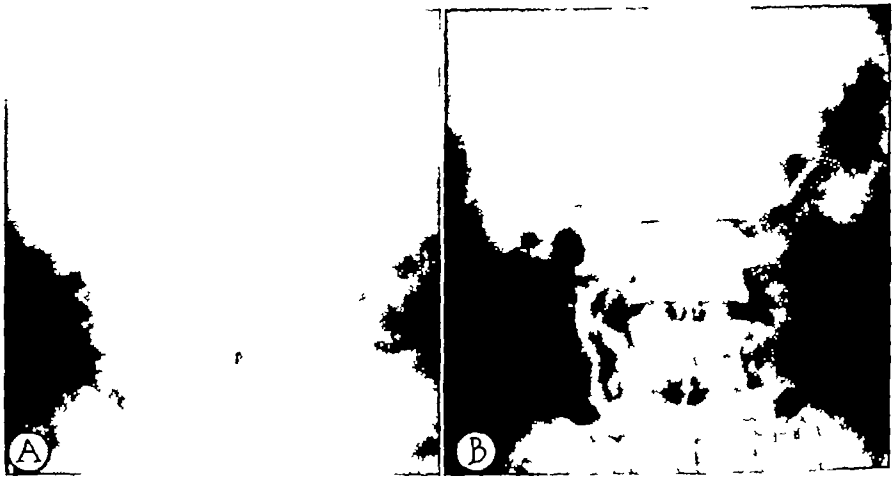


FIG 9 Case 3 J M, man aged 31 *A*, intravenous pyelogram shows hydronephrosis and hydroureter of remaining kidney, associated with healed, contracted tuberculous bladder (May 1953) Ureteroileocystoplasty done May 27, 1953 *B*, intravenous pyelogram (June 11, 1956), there has been a return to normal of kidney and ureter

also the loop, are only partly emptied of medium at the end of micturition, the proximal part of the loop (on the patient's left) is almost completely empty (fig 13, *B*) but the distal part of the loop is still full to capacity (or it may even be distended) Nevertheless the upper tract is still normal, though a slight reflux goes halfway up the right ureter This finding of the imperfect emptying of the distal horn of the U-shaped loop suggests that it would be better to join the ileal loop to the bladder, at or near to its distal end It has also been shown that the *ring-plastik* of Scheele (1941) is not free from the defects of residual urine and perhaps should be avoided (Hanley 1956)

It seems, therefore, that the remodeling of the contracted bladder by incorporating in it intestinal muscle of different contractile power and discipline, is usually a successful procedure but it does not achieve in every case the power of a perfectly integrated contraction It is not yet certain whether this defect applies more to the tiny bladders than to those bladders which are merely small

In some cases with high residual urine following ileocystoplasty, for tiny tuberculous bladders, Cibert (1956) has found it necessary to resect the bladder neck to assist complete evacuation

Electrolytes No instance of electrolyte imbalance has been noted and no medical treatment by alkalies has been advised Table 3 shows examples of postoperative electrolyte studies in a group of cases As we found in our early experimental studies, any so-called reservoir effect from electrolyte absorption has not been clinically or biochemically detectable

Infection Nearly every case has sterile urine within a few weeks of the operation

Ileocystoplasty using an open ileal loop I have used the operation of ileocystoplasty using an open loop in one case of carcinoma of the bladder in a woman aged 65, in which I had done a very large partial cystectomy The ileal loop was

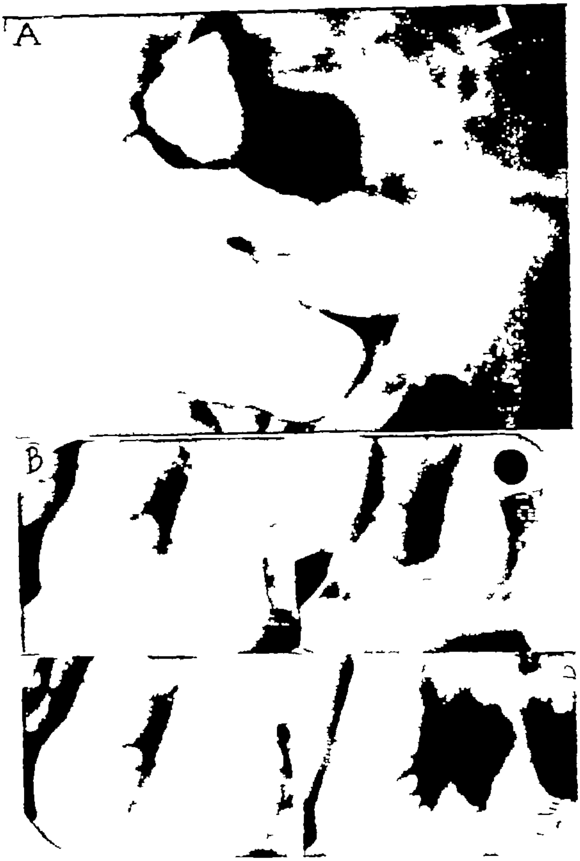


FIG 10 A typical retrograde cystogram following ileocystoplasty Opening between bladder and loop remains widely open, loop fills well with opaque medium *B* serial x-rays studies of ileal loop in case of ileocystoplasty Radiographs have been taken at intervals of a few seconds Pictures show irregular outlines demonstrating peristaltic activity, there are phases of marked contraction and dilatation of different parts of loop

prepared in the usual way both ends being left open it was then divided completely along the antimesenteric border and the bleeding points were ligated The flat graft thus obtained was sewn to the cut edges of the bladder to enlarge it There was a slight leakage of urine from the fourth to the tenth day but the patient died unexpectedly from pulmonary embolism on the fourteenth day This technique using the open loop involves longer suture lines than the operation with the closed loop to which operation I think it is inferior (Pyrah and Raper 1955)

Tasker (1953) utilized an open ileal graft to enlarge the bladder of the dog and also in one man with a contracted bladder He used an isolated loop of ileum eight inches in length that was divided into two portions which were then opened along their antimesenteric borders the two open loops were then stitched together laterally thus making a flat rectangular graft three by four inches in

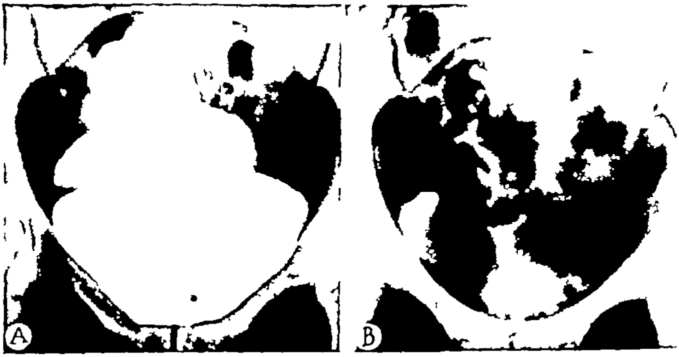


Fig 11 Case of ileocystoplasty for healed, contracted, tuberculous bladder, there is practically complete emptying of bladder and loop after voluntary voiding

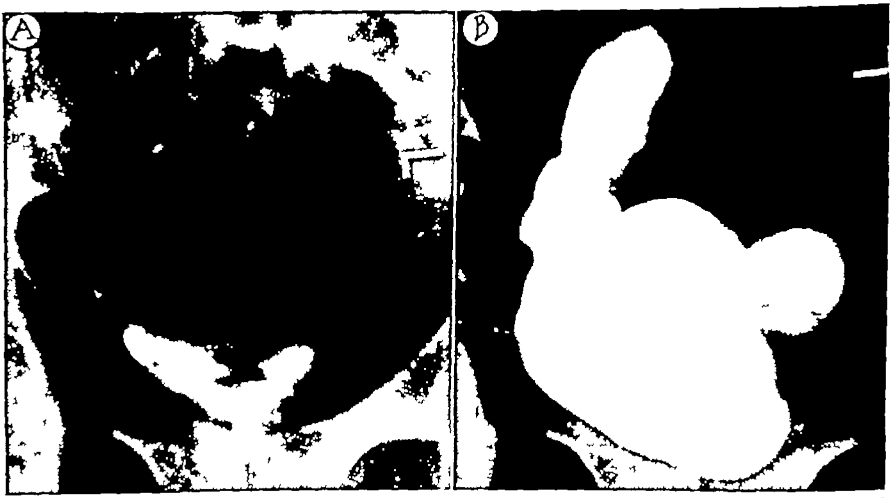


Fig 12 Case of ureteroileocystoplasty for small bladder resulting from longstanding tuberculous cystitis, there is very small amount of residual urine after voluntary voiding

size The bladder was then bisected in the median sagittal plane from front to back, thus making an elliptical opening, to the edges of which the flat, rectangular, ileal graft was sutured by two rows of stitches The end results in the dogs and also in the man, were satisfactory and gave a bladder which contracted well with very little residual urine

ILEAL BLADDER AS A RESERVOIR COMPLETELY REPLACING A NORMAL BLADDER (ILEOURETHRAL ANASTOMOSIS)

It is sometimes possible to construct a complete "bladder" made from ileum and draining per urethram, after the patient's own bladder has been excised Since the new muscular organ is free from feces, it should remain free from infection, and since absorption of chloride and sodium from the ileum is low quantitatively and in equivalent amounts (Pyrah, Care, Reed and Parsons, 1955), if the kidneys are healthy, the fact that the ileum is now a "reservoir" as distinct from a "conduit" should not prove detrimental

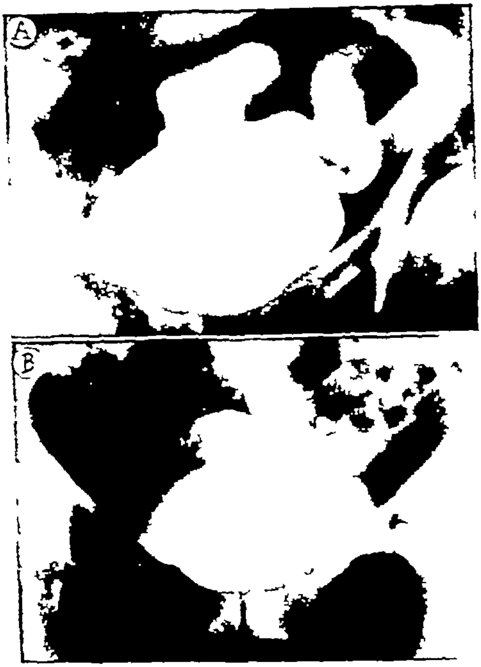


FIG. 13. Retrograde cystogram in case of ileocystoplasty. *A*, bladder and loop are well filled. *B*, cystogram after voiding. Bladder has been only partially emptied (medium in bladder is less dense than that shown in *A*), proximal part of loop is emptied but distal part of loop is still well filled.

TABLE 3. *Blood electrolyte levels following ileocystoplasty in six cases*

Patient	Operation	Time after Operation	Postoperative				
			Blood urea (mg per 100 cc)	Sodium (meq/L)	Potassium (meq/L)	CO₂ combining power (meq/L bicarb.)	Chloride (meq/L)
A. N.	Ileocystoplasty	1 yr 11 mos	17.0	139	3.7	24.5	99.2
T. M.	Ureteroileocystoplasty	14 mos	13.4	145	4.5	24.2	109
K. M.	Ileocystoplasty	4 mos	13.4	135	4.6	24.5	106
N. B.	Ileocystoplasty	4 yrs 3 mos	25.2	141	4.5	25.7	99.2
E. P.	Ileocystoplasty	4 yrs 6 mos	25.0	135	4.3	31.5	96.5
J. M.	Ureteroileocystoplasty	3 yrs 1 mo	23.7	145	5.4	32.5	102.5

The first attempt at such a procedure was that of Couvelaire (1951) who, after removing the bladder for carcinoma, anastomosed the side of the lower end of a loop of ileum to which the ureters had been joined to the prostatic urethra; the upper end of the ileal loop was brought to the surface of the abdomen as a temporary ileostomy. After some unsuccessful attempts the ileostomy opening was eventually closed when urethral voiding occurred; some straining and gentle manual pressure over the lower abdominal wall assisted micturition.

I have carried out the operation of total substitution of the bladder by ileum using a different technique, in two patients with carcinoma of the bladder, and my colleague, Mr Raper, in one case for recurrent Hunner's ulcer In my first case the operation was successful, the second patient died from pulmonary embolism four weeks after operation after having had a normal convalescence, autopsy showed a satisfactory technical result

Case 4 My first patient, a man aged 45, had had multiple low grade papillary carcinomas for some years which had been treated in succession by per urethram diathermy or resection and by radium placed in the center of a distended Foley catheter, the latter treatment was later followed by persistent and severe hematuria (which necessitated transfusion), caused by a radio-necrotic ulcer in the vault and lateral wall of the bladder, the bleeding from which could not be permanently controlled The bladder, the seminal vesicles and the proximal two thirds of the prostate were removed transperitoneally, the prostate being sectioned transversely so as to leave a stump consisting of the apex of the gland, in order to enable the urethra to be anastomosed to the ileum (fig 14) A loop of ileum 22 inches in length was prepared in the manner previously described, and the ureters, having been divided at the pelvic brim, were joined by a direct mucosa-to-mucosa technique to the ends of the loop which were then invaginated so that the ureteroileal anastomosis was on a small eminence within the lumen The center of the ileal loop was anastomosed to the prostatic urethra, the broad stump of the prostate being of sufficient size to allow two rows of sutures to be used The first row of stitches secured the seromuscular coat of the ileum to the fibromuscular wall of the stump of the prostate posteriorly, a small opening of a size equal to that of the urethra was then made into the lumen of the ileum through all coats to enable an ileourethral anastomosis by mucosa-to-mucosa apposition to be made, finally the seromuscular coat of the ileum was sutured to the prostate anteriorly A catheter was retained in the urethra 10 days A slight leakage of urine for the first four days did not retard his progress, the urethral

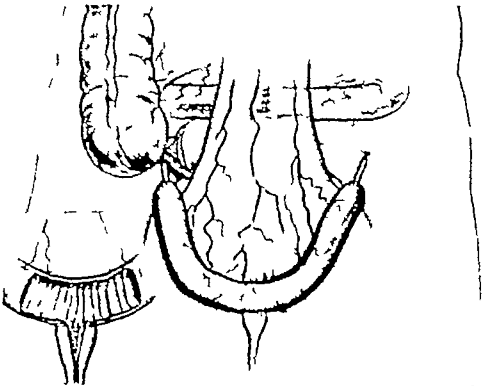


FIG 14 Case 4 G S, man aged 45 Bladder, seminal vesicles and proximal two-thirds of prostate were excised for carcinoma of bladder Bladder was replaced by long loop of ileum which was anastomosed at its middle to prostatic urethra Divided ureters were joined to ends of loop

catheter was removed on the tenth postoperative day and normal micturition was established (Pyrah 1956)

The patient soon learned to recognize when the new bladder was distended and partly by gentle straining and partly by exerting a little manual pressure over the lower part of the abdomen, easy voiding, somewhat lacking in normal force, followed He gained complete control of micturition during the day but had slight urethral leakage at night The postoperative cystogram showed the bladder distended with opaque medium and the absence of ureteric reflux, when the bladder was emptied a small amount of residual urine remained The intravenous pyelograms showed no dilatation of the upper urinary tract three months after operation The urine remained sterile There was no hyperchloremic acidosis the blood electrolyte figures being as follows sodium 145 meq/L, potassium 4 1 meq/L, chloride 102 5 meq/L, CO_2 combining power 26 6 meq/L Some weeks after operation the patient returned to work as an engineer Ultimately a recurrent growth developed in the left side of the stump of the prostatic urethra, and proved fatal exactly two years after the original operation The ileal bladder continued to function until the end The case illustrates the difficulty in the selection of cases for such a procedure, having regard to the bladder tumor and its possible late spread, this case was selected because there seemed to be a reasonable chance that the malignancy had been cured, the main residual defect being the large, bleeding, radio-necrotic ulcer

Mr Raper's patient, a man aged 45, first had a particularly painful Hunner's ulcer for which partial cystectomy and ileocystoplasty were carried out, these procedures were followed later by a recurrent ulcer in the residual portion of the bladder and further persistent pain The operation which I have described was then successfully performed and the patient is still alive

LOOP OF ILEUM AS A URINARY CONDUIT TO THE EXTERIOR

The externally draining isolated ileal loop, used as a conduit to the exterior (variously called the ileal bladder or ileal segment or ileal ureterostomy), has been used in certain cases requiring deviation of the stream because of urinary incontinence in which, because of an incompetent or destroyed anal sphincter, ureterocolic anastomosis has been contraindicated, the isolated rectosigmoid bladder is also impracticable in such cases The procedure has also been advocated by Bricker (1947) in association with a colostomy, following pelvic exenteration for advanced pelvic cancer, as an alternative to a wet colostomy over which it has advantages The conditions shown in A in table 4 (the cases done in my department) appear to be firm indications for the use of this operation when other methods of controlling the incontinence have failed I shall refer later to the use of the ileal bladder as a primary method of urinary diversion in cases requiring total cystectomy for bladder cancer and as a revision procedure in certain cases of failed ureterocolic anastomosis

Literature Bill, Dillard, Eggers and Jensen (1954) successfully constructed isolated ileal segments in two children aged 16 months and three years for ectopia vesicae with bilateral hydronephrosis and spina bifida respectively In both cases

TABLE 4 *Ileal bladder (ileal segment or ileal ureterostomy)*

	Cases	Deaths
A		
1 Spinal injury	1	
2 Spina bifida	11	3
3 Vesicovaginorectal fistula	3	
4 Pelvic evisceration	1	
5 Late cases of ectopia vesicae	2	
B		
6 Bilateral hydronephrosis	1	1
7 Revision or ureterocolic anastomosis	3	
C		
8 After cystectomy for carcinoma	5	3
	—	—
	27	7

the hydronephrosis was much improved and in the second, recurrent attacks of ascending renal infection were controlled No electrolyte imbalance developed after operation

Nash (1956) reported 10 cases of ileal bladder for spina bifida with good results, nine had had previous operations on the bladder in an attempt to relieve their urinary incontinence Rickman (1956) recorded a series of 15 children in whom he had used ileal loop external drainage, there were five cases of spina bifida, between the ages of sixteen months and ten years, 2 cases of chronic urethral obstruction aged nine and 10 respectively, and one case each of postoperative urinary and fecal incontinence and of megaureter with hydronephrosis, there were two operative deaths The end results were very good, the patient having satisfactory pyelograms and normal blood electrolytes, the urine was usually sterile within a fortnight

Spina bifida Spina bifida is the commonest indication for ileal loop drainage in this group Many children with spina bifida live in institutions for cripples because of paralyses of the legs and incontinence of urine and feces These children commonly have defective sensation in the limbs and in the saddle area, and often ulceration of the skin and of the genitalia as well which add to their state of misery Some have meningoceles The continuous drainage of urine makes them social outcasts Other cases, less severe, have urinary and fecal incontinence as their principal defect and no paralysis of the legs The incontinence of feces, often partly compensated for by severe constipation, is dependent upon a paralyzed external anal sphincter, so that ureterocolic anastomosis cannot be done to relieve the urinary incontinence

The cause of the urinary disability in these children varies and the surgical measures undertaken to remedy the defect often still leave the patient with no urinary control Some cases have had, at first, urinary retention due to a thick, hypertrophied, internal sphincter and in these resections of the bladder neck may be partly or wholly successful in relieving residual urine, though sometimes they leave the patient more incontinent than before In other cases the bladder neck is wide open with no sphincteric control and for such patients sling operations or other plastic procedures may have been tried, often with indifferent results Complete transection of the bladder neck with urethral closure and suprapubic drainage usually leads to infection and sometimes to stone formation Bilateral ureterostomy, the orifices being surrounded by a strap-like skin graft to form nipple-like eminences, has probably offered the best chance of control of the urinary incontinence with the help of an appliance, prior to the introduction of the ileal bladder

The use of the ileal bladder or ileal segment in these incontinent children, especially after they have been rendered mobile by the use of orthopedic appliances, has been the best measure so far devised to give them urinary control and has allowed them to continue their education and has placed them many steps nearer to gainful employment

The operation The loop, seven or eight inches in length, is isolated as previously described, and intestinal continuity is restored by end-to-end anastomosis, too short a loop which may contract lengthwise or may lead to tension at the stoma or at the ureteral anastomoses, should be avoided The ureters are exposed, ligated just below the brim of the pelvis, and divided The left ureter is usually brought through an opening in the base of the mesosigmoid to a position nearer the midline and after slitting it up to give an elliptical opening, is anastomosed either end-to-end with the ileum, using a continuous through-and-through suture, reinforced by interrupted stitches of finest catgut uniting the peritoneal coat of the intestine to the fibrous covering of the ureter, or alternatively it is joined to the ileum by mucosa-to-mucosa suture near to the closed proximal end of the loop at its antimesenteric border (fig 15) The right ureter is brought below the ileal loop and similarly anastomosed

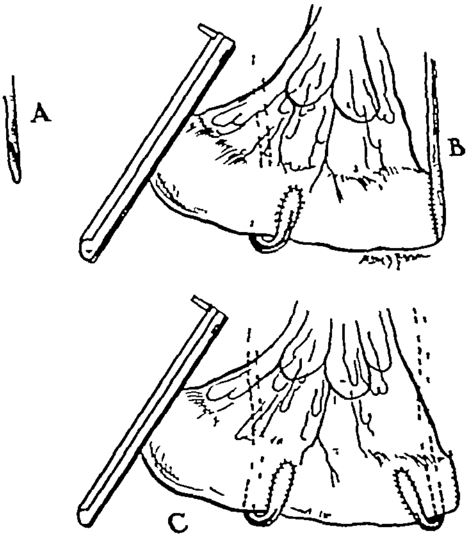


Fig 15 Diagram shows two alternative methods of anastomosis of ureter to isolated ileal loop, used in children with spina bifida, direct mucosa to mucosa anastomosis is used, ureters being given an elliptical terminal opening

to it some three inches from its proximal end The direct mucosa-to-mucosa anastomosis is preferred to the Coffey method because in the absence of any build-up of backpressure or of feces, it appears to be safe, and it provides a free drainage of urine and avoids anastomotic stricture The proximal part of the ileal loop is secured to the posterior parietal peritoneum and the ureteric anastomoses are covered by peritoneum, to prevent herniation of intestinal contents, the distal part of the intestinal loop may be secured to the peritoneum of the right iliac fossa, or be brought straight forward to the final position of the stoma The ileostomy opening is placed in the right iliac fossa near McBurney's point after excising an ellipse of skin and aponeurosis so as to avoid lateral pressure upon the protruding ileum, an inch or more of which is allowed to prolapse through the opening, the everted mucosa being then sutured to the skin margins A Rutzen's ileostomy bag is secured to the surrounding skin before the patient leaves the operating theater

The operation has carried a mortality from intestinal obstruction and ileus in our series of 3 cases, out of 11, which is indicative of the severity of the procedure, but the latest cases in the series have withstood the procedure well

Late results These patients have benefited greatly by the operation We have not so far encountered any stomal contraction with the technique which we have used Electrolyte imbalance has not occurred and so far no attacks of renal infection, and no cases have needed treatment by alkalies Table 5 shows normal postoperative blood electrolyte figures in a group of cases at varying times after operation The late pyelograms have usually been normal, though for some time after operation there may be transient hydronephrosis, and in cases with a preoperative hydronephrosis, improvement has followed the operation (fig 16)

THE USE OF INTESTINAL SEGMENTS AS A METHOD OF URINARY DIVERSION

I will now refer to the use of isolated segments of the large and the small intestine as a method of urinary diversion, alternative to the operation of uretero-

TABLE 5 *Blood electrolyte readings in cases of ileal bladder (ileal segments or ileal ureterostomy)*

Patient	Diagnosis	Time after Operation	Postoperative				
			Blood urea (mg per 100 cc)	Sodium (meq/L)	Potassium (meq/L)	CO_2 combining power (meq/L)	Chloride (meq/L)
D C	Spina bifida	4 wks	21 0	135 0	4 2	25 9	94 0
G M	Spina bifida	4 wks	22 0	141 0	4 3	30 6	99 0
A J	Revision after U C A	12 mos	25 0	141 0	4 2	24 9	106 0
P P	Revision after U C A	8 mos	38 0	137 0	4 8	24 9	106 0
G H	Spina bifida	7 mos	32 0	145 0	4 3	24 5	104 2
H C	Vesicovaginal-rectal fistula	16 mos	24 2	145 0	4 3	27 4	107 8
A W	Cystectomy	6 mos	20 3	139 0	4 0	20 3	104 2
J S	Pelvic evisceration	20 mos	18 1	137 0	4 8	27 0	106 0

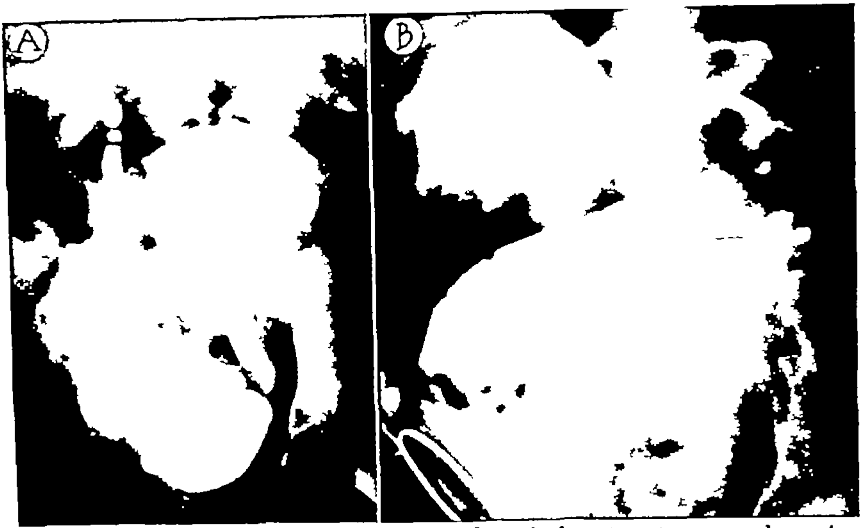


FIG 16 Case of spina bifida in boy of six for whom ileal ureterostomy was done *A*, preoperative bilateral hydronephrosis and hydroureters (January 31, 1957) *B*, five weeks after operation (March 3 1957) intravenous pyelograms showed normal upper urinary tract Rutzen bag and belt are in position

colic anastomosis, but first I will sketch in the background to these procedures by giving some late results of the operation of ureterocolic anastomosis

URETEROCOLIC ANASTOMOSIS

The operation of ureterocolic anastomosis has come under criticism firstly because there is an important early and late incidence of renal deaths from ascending infection, which are quite independent of the primary disease (cancer, trauma or tuberculosis) for which the patient was treated, and secondly because, although many survivors are extremely fit, others enjoy health which is not quite first class and a few are renal invalids who require revision operations if they are to survive

In addition to there being a postoperative incidence of renal deaths, there is an important late incidence In an analysis of the cause of death by period of survival following ureterocolic anastomosis, on behalf of the British Association of Urological Surgeons, Jacobs and Stirling (1952) found that of 1,029 deaths at various times after operation, 298 died from recurrent cancer while there were 301 renal deaths, of the renal deaths approximately one-third died in less than four weeks after operation, one-third in from one to six months after, and one-third from six months to 10 years following operation (table 6) These statistics which highlighted the mortality from renal infection, were collected shortly after the papers by Ferris and Odel (1950) and other workers in this field (Lapides 1951, Parsons, Powell and Pyrah, 1952, Parsons, Pyrah, Powell, Reed and Spiers, 1952) had drawn attention to the two mechanisms involved in the renal deaths, namely the ascending infection and the electrolyte imbalance so that present-day results are probably better

TABLE 6 *Ureterocolic anastomosis, 1,029 deaths Cause of death by period of survival (Jacobs and Stirling, 1952)*

Cause of Death	Under Four Weeks per cent	One to Six Months per cent	Six Months to Ten Years per cent	Total
Carcinoma	5 7	31 9	62 4	298
Renal	32 2	30 6	36 2	301

TABLE 7 *Cases of ureterocolic anastomosis, 39 surviving cases*

With cystectomy for cancer	28
For traumatic conditions	4
For contracted bladder	7
	39

Grade of health

Grade	Cystectomy for Cancer and Traumatic Cases	T B Transplants	Total
Grade 1	19	2	21
Grade 2	8	2	10
Grade 3	1	2	3
Grade 4 (failed cases)	5		5
			39

Status of separate renal units in 28 surviving cases of total cystectomy plus ureterocolic anastomosis and 2 traumatic cases
(T B transplants and failed cases excluded)
(56 renal units)

No hydronephrosis	32
Slight hydronephrosis	8
Moderate hydronephrosis	11
Severe hydronephrosis	5
	56

(Various techniques)

In addition to the toll of renal deaths it became clear that although many patients make excellent long-term recoveries, some survivors do not enjoy first-class health (because of mild renal infection and electrolyte imbalance) although they do not necessarily die, and a few are on the edge of a renal breakdown I will illustrate the variations in the quality of the late results by referring to the grade of health and some of the disabilities of a group of 39 surviving patients in my department who have had ureterocolic anastomosis, the renal status after operation of 28 surviving cases is also given (table 7)

In grade 1 are placed those patients with very good health, with a good appetite, an absence of thirst, with the ability to do the day's work without loss of time, with no renal symptoms and with normal postoperative pyelograms or with one normal pyelogram and one showing slight hydronephrosis and with no or slight acidosis In grade 2 are placed those who are clinically well and able to work whose pyelograms are normal or show some hydronephrosis, and who have some hyperchloremic acidosis which is readily corrected by alkali and who have therefore had some renal infection but when they are questioned some of these have restrictions in their diet and long-term survivors may even have osteoporosis Table 7 places 31 of the 39 cases in grades 1 and 2 and these can be accounted satisfactory operative results though as I have indicated, some in grade 2 have health which is just short of the best In grade 3 are placed patients who are not perfectly fit, having had some renal damage, but who yet may be able to work some have more or less stable health but others have periods of vague ill-health these patients need very careful after-care and the long-term prognosis would seem to be poor Grade 4 consists of cases in which the ureterocolic anastomosis has been a failure a small group who have had recurrent attacks of infection with electrolyte imbalance, so severe that it seemed that they must die from renal failure, in these cases some form of revision procedure was needed in order to save life Table 7 places eight of the 39 cases in these two groups of unsatisfactory results

What variations from normal health cause patients to be graded 3 and 4 (and occasionally grade 2) and how can their disabilities be corrected? The next few cases will illustrate

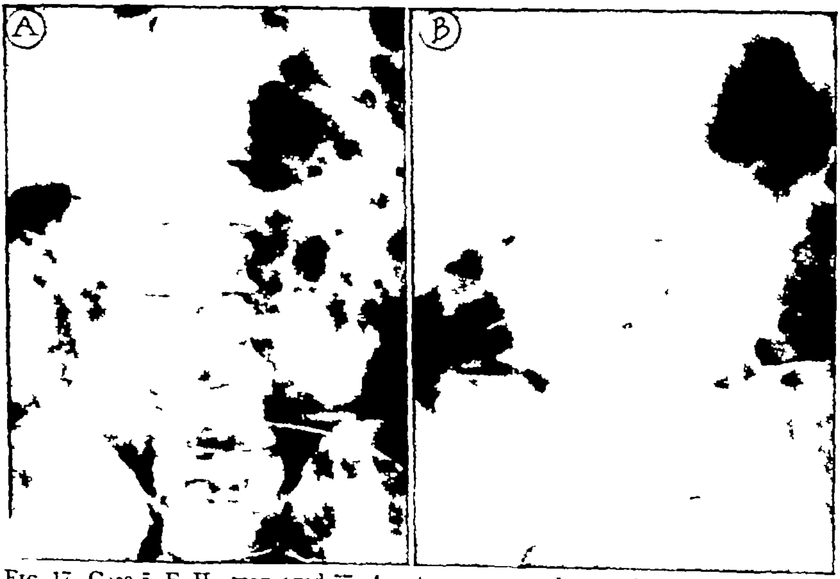


FIG 17 Case 5 F H man aged 57 A intravenous pyelogram before cystectomy (November 25 1954) no secretion from left kidney, *B* postoperative intravenous pyelogram 3 months after operation (April 6, 1955) Function has returned to left kidney pyelograms within normal limits

Case 5 Figure 17 shows the pre- and postoperative normal pyelogram of a man, aged 57, who had total cystectomy and ureterocolic anastomosis in January 1955, for an extensive transitional-cell carcinoma of the left side of the bladder His health appears to be very good indeed, he has normal appetite, normal energy and no complaints, he takes sodium bicarbonate and his blood electrolytes are normal (table 8) Everything points to this man's having had a first-class result But when recently he had metabolic balance tests, and was given a loading dose of sodium chloride and a restricted potassium intake, in five days he began to feel not quite so well because the kidneys could not excrete the excess chloride ions, whereas they excreted too much potassium, he was found, in fact, to have a total body deficit of potassium Although, therefore, his renal excretory mechanism (as shown by the intravenous pyleograms and the blood

TABLE 8 *Postoperative blood electrolyte studies*

Case F H W H Age 57 ♂	Preoperative		Postoperative Chemistry				
Dates	28/10/54	1/4/55	20/1/55	3/3/55	5/5/55	6/2/55	25/8/55
Cl, meq/L	100		99 2	107 8	99 2	97 4	100 9
CO c p meq/L	24 2		28 3	26 2	29 2	27 4	27 8
Na, meq/L	135	Operation	135	133	141	137	143
K, meq/L	4 6		4 0	3 8	5 4	4 6	4 5
B U N , mg %	29 4				29 4	35 2	34 4

TABLE 9 *Pre and postoperative blood chemistry of a man aged 72 who had cystectomy with ureterocolic anastomosis on April 4, 1955 He had electrolyte imbalance with clinical symptoms, resulting from attacks of renal infection Improvement followed his taking a low chloride diet together with alkalies*

Case G B Age 72 ♂	Pre-operative		Postoperative Chemistry				
Dates	10/2/55	4/4/55	8/11/55	6/10/55	1/12/55	23/2/56	19/4/56
Cl, meq/L	102		111 1	109	118 0	114 5	104 2
CO c p , meq/L	27 2		21 9	22 8	18 5	19 8	25 3
Na, meq/L	133	Operation		143	137	139	135
K, meq/L	6 2		4 2	4 7	5 3	4 5	4 6
B U N , mg %	21 3				31 0	30 2	33 5

TABLE 10 *Prohibited foods Hyperchloremic acidosis*

- Tinned, salted and prepared meat or fish
- Cheese (except home made salt free)
- Tinned vegetables, soups and fruit
- Pickles and bottled sauces
- Extracts of meat and yeast (e g bovril)
- Breakfast cereals, *except* salt free porridge
- Bread—limited to 6 ozs per day
- Daily intake of milk—½ pint

urea nitrogen) is only slightly impaired, and although his imbalance is readily corrected, he is, in fact, not far removed from a very troublesome homeostatic imbalance because of a renal tubular defect, and from the biochemist's point of view he is considerably removed from normal He is dependent on medical after-care

The blood electrolyte figures of a man aged 72 who had cystectomy and ureterocolic anastomosis in 1955, with a very persistent electrolyte imbalance from attacks of recurrent renal infection are shown in table 9 His health was eventually greatly improved (his appetite became good and his thirst disappeared), when, in addition to being given alkalies, and being advised to abstain from salt as a condiment, he was given a low-chloride diet in order to reduce his total body chlorides (table 10)

The radiographs are shown in figure 18 of some of the bones of the legs of a man of 58 with a generalized osteoporosis causing pain in the back the pelvis and the thighs resulting from long-standing hyperchloremic acidosis He had ureterocolic anastomosis in 1942 for hydronephrosis of a solitary kidney with impaired function, caused by a severely contracted tuberculous bladder He has worked for almost the whole of the last 14 years Since 1952 his acidosis has been corrected by alkalies There is still a risk that he will get a spontaneous fracture of a long bone

The following three cases record revision procedures done for ureterocolic anastomosis that failed

Case 6 A woman aged 42 had ureterocolic anastomosis in 1951 for a very large vesicovaginal fistula which had followed the sloughing of the anterior vaginal wall after an operation for prolapse in 1944, for which several unsuccessful attempts at repair had been made elsewhere In the 18 months following ureterocolic anastomosis she had a number of attacks of acute pyelonephritis with elec-

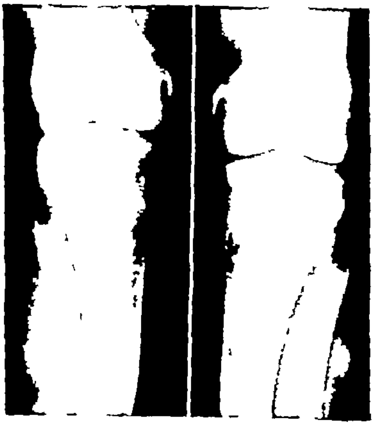


FIG 18 Case 7 H M man aged 58 had ureterocolic anastomosis in 1942 for solitary hydronephrotic kidney resulting from contracted tuberculous bladder Radiograph (January 1954) shows osteomalacia (best shown in long bones) resulting from long standing acidosis (By courtesy of British Journal of Urology vol 29, p 45 1957)

trolyte imbalance, which were associated with such marked invalidism that her kidneys were endangered It was then noticed that the vesicovaginal fistula had contracted very much, probably because no urine was now passing through it In view of the threatened danger to the kidneys, the fistula was closed in April 1953, and six months later both ureters were reimplanted into the bladder, using a U-shaped ileal loop, the center of which was anastomosed to the bladder, the ureters being attached to the ends of the loop (fig 19) This patient is now fit, the urine is sterile and she had had no further attacks of renal infection, there is very little residual urine Her blood electrolyte levels are normal although a length of ileum about fourteen inches long has been incorporated into the urinary tract The revision procedure had been urgently needed

Case 7 A man aged 58 had had several operations by another surgeon for a

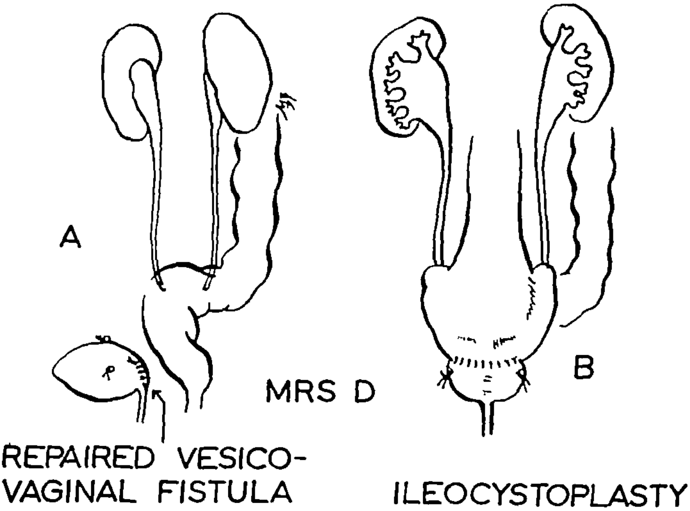


FIG 19 Case 6 M D, woman aged 42, underwent bilateral ureteroileocystoplasty as revision procedure for failed ureterocolic anastomosis

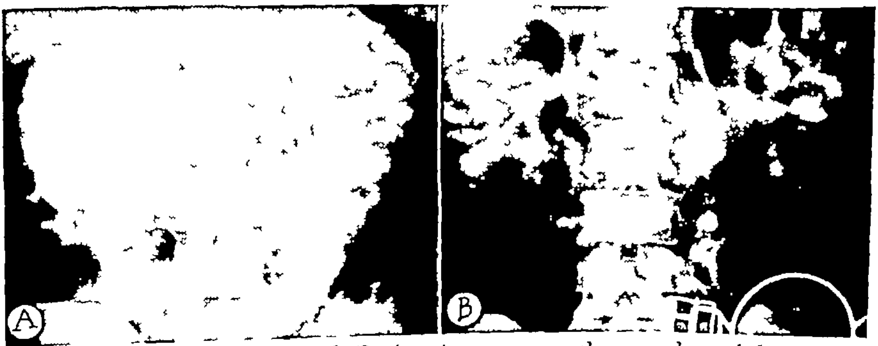


FIG 20 Case 7 P P, man aged 58 *A*, intravenous pyelogram shows bilateral hydronephrosis in case of failed ureterocolic anastomosis (September 1954), first revision procedure gave only slight improvement *B*, intravenous pyelograms one month after second revision procedure (March 10, 1956), an ileal ureterostomy, note great improvement in hydronephrosis

severe stricture of the urethra for which in the end he had performed ureterocolic anastomosis The operation was a failure, since the patient developed bilateral hydronephrosis and hydroureter (figs 20 and 21) and recurrent attacks of ascending infection, so severe and persistent that for 12 months he was almost completely absent from work It was suggested to me by his doctor that the ureters should be reattached to the bladder I first excised the urethral stricture, joining the ends together, and later rejoined the two ureters to the bladder using a U-shaped ileal loop (January 1955) Some residual urine still persisted, however, and it was never possible to free the urinary tract from the original infection (which was now shown to be caused by Pseudomonas pyocyaneus) and which proved refractory to all antibiotic and antiseptic treatment, the hydronephrotic kidneys did not improve and further severe and prolonged attacks of pyelonephritis followed in the next 12 months, necessitating further absence from work In January 1956, I substituted for the new anastomosis, an ileal ureterostomy (or ileal segment) (fig 21) The hydronephrosis has been greatly reduced (fig 20, *B*), he has had no further attacks of infection and he has been able to work without loss of time for the last 12 months The blood electrolytes are normal though his blood urea nitrogen (because of his damaged kidneys) is somewhat elevated The operation has been life-saving

Case 8 A woman aged 33 had bilateral ureterocolic anastomosis in March 1952, for a urethrovesicovaginal fistula The operation was never clinically

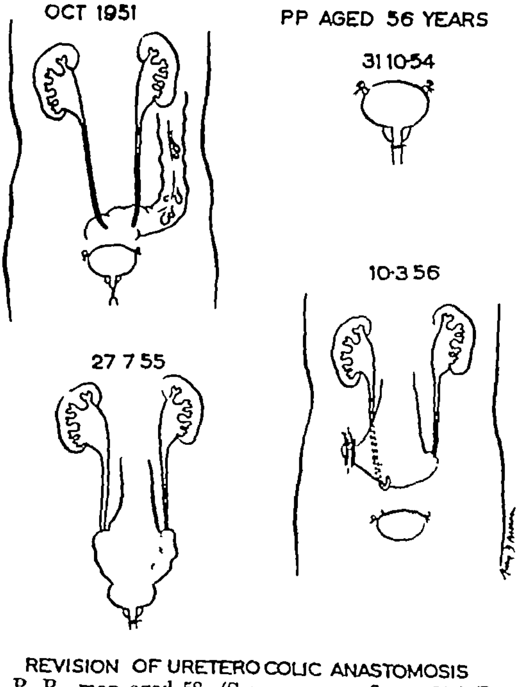


Fig 21 Case 7 P P, man aged 58 (Same case as figure 20) Diagram shows various operations

satisfactory since it was followed by recurrent attacks of right renal pain with temperature which ultimately necessitated the removal of an infected right kidney After an interval, there followed further attacks of left renal pain, and temperature which were *accompanied by an unusual form of electrolyte* imbalance consisting of a hypokalemia associated with painful attacks of tetany of the hands and feet which we failed to control Seven months later, in September 1955, the left ureter was anastomosed to an isolated ileal segment since when the patient has been symptom-free and has enjoyed normal health

This brief appraisal of some results of the operation of ureterocolic anastomosis has included an account of some of the *failures* and of the salvage procedures which have been done to save lives I believe, however, that the late results of the operation are better than those of a few years ago because of improved techniques and especially because of a better understanding of the medical after-care, which must be accepted by patient and surgeon as a necessity for those who have this operation

ALTERNATIVE METHODS OF URINARY DIVERSION USING INTESTINAL SEGMENTS

In the search for a method of urinary diversion which would give more uniformly satisfactory results than ureterocolic anastomosis, some surgeons have transplanted the ureters into isolated segments of intestine, using the ileocecal region, the rectosigmoid, and the terminal ileum These methods have been used either in selected cases or by some surgeons as a routine

ILEAL BLADDER (ILEAL SEGMENT, ILEAL URETEROSTOMY)

The ileal bladder (or ileal segment, or ileal ureterostomy), prepared as previously described, has been advocated by Bricker (1947, 1954) and by Wells (1953, 1956) as a satisfactory alternative method of urinary diversion following cystectomy for carcinoma of the bladder, and it is at present under trial The ileal ureterostomy in such cases is not a reservoir but a simple conduit for urine draining continuously to the exterior, the stoma in the abdominal wall not being guarded by any sphincter When ileal ureterostomy is combined with cystectomy for bladder cancer the results and the efficiency of the procedure must be compared with those of the rectosigmoid bladder, in order to command general acceptance

In my department, because of my own personal preference for the rectosigmoid bladder, we have only used the ileal bladder along with cystectomy for bladder cancer, in eight cases *including three revision procedures, two of which* have already been referred to, so that the series is too small for an assessment of its value

I will therefore refer to the series recently collected by Professor C A Wells for the British Association of Urological Surgeons In that series, of the 92 cases of ileal ureterostomy and cystectomy for cancer of the bladder, operated upon by various surgeons, there were 29 deaths in hospital (or 30 per cent), in addition eight of nine cases died in which ileal ureterostomy alone was done as a palliative procedure The corresponding figures by Annis (1956), who reported the Liverpool series, were 10 deaths in 41 patients (25 per cent), while Bricker and associates (1954) had a mortality of 14 per cent in 106 cases, of which 81 were cases of pelvic evisceration, 16 were cystectomies and 9 were palliative operations for bladder cancer and other indications The operation, therefore, in such patients is considerably more serious than the corresponding operation in children with spina bifida, in whom it has been relatively well borne

The complications in hospital in the British series revealed a high postoperative morbidity, of 209 patients having ileal ureterostomy from all causes, 120 had complications, which included ileus (42 cases), urinary fistula (20 cases), mechanical intestinal obstruction (10 cases) and burst abdomen (13 cases)

The state of health and well-being of survivors has been remarkably good, with little late morbidity and little need for medical after-care, though occasional patients have developed stomal contraction, which should be correctable with changed techniques

In Wells' (1956) series of cases of ileal ureterostomy, there was an elevated serum chloride in 23 per cent of 96 cases and CO_2 combining power lower than normal in 52 3 per cent of 86 cases in which figures were available These figures are surprisingly high since Bricker and associates (1954) in 65 patients found an elevated serum chloride at any time after operation, in only 2 patients, and both cases had had the operation performed as a revision procedure for previous ureterosigmoidostomy, the kidneys being infected In our own series of cases of ileal ureterostomy for spina bifida, hyperchloremic acidosis was not found

When the mucosa-to-mucosa technique of ureteroileal anastomosis was used the incidence of postoperative hydronephrosis was low and patients having preoperative hydronephrosis nearly all showed improvement (Bricker and associates, 1954, Wells 1956)

Ascending renal infection, though the incidence is not high, does exist Wells (1956) recorded pyelitis in 11 of 156 patients for whom ileal ureterostomy had been done for any cause, and since the series included a few revision procedures in patients with infected kidneys following ureterocolic anastomosis this incidence is very low In 65 patients with ileal ureterostomy carried out as part of the procedure for pelvic exenteration for pelvic cancer and surviving for longer than six months, Bricker and associates (1954) found that eight cases had intermittent pyelonephritis and a further four had pyelonephritis with hydronephrosis none, however, had died of pyelonephritis

The operation of ileal bladder or ileal ureterostomy in association with total cystectomy, therefore, while giving satisfactory results in survivors, is a serious operation carrying a considerable operative mortality and morbidity

ILEOCECAL BLADDER

Mernicks (1955) has used the ileocecal bladder as an alternative method of urinary diversion in 31 patients The ureters were transplanted into a new "bladder' consisting of eight inches of isolated cecum and ascending colon nine inches of terminal ileum are included to act as an ileal urethra, the ileocecal valve preventing regurgitation of urine Continuity of the gut is restored by ileo-transverse colostomy Serious infection has occurred in one patient and electrolyte imbalance in two After using an indwelling catheter for the first few preoperative days, a catheter is passed at three- to four-hourly intervals to empty the bladder, this is a disadvantage as infection may sooner or later be introduced, leading to pyelonephritis Merricks (1955) recommends daily dilatation of the new "bladder" with water for the first three months in order to achieve a capacity of 300 to 500 ml The operation is an extensive procedure, adding the risks associated with an intestinal anastomosis to those of the ureterocecal anastomoses

THE RECTOSIGMOID BLADDER

The idea of the isolated rectosigmoid bladder was first described by Mauclaire in 1895, though it has been little used since that time I have used this procedure combined with total cystectomy for bladder growths, in 20 cases The first 4 cases were done in 1952 when some ureterocolic anastomoses using a direct mucosa-to-mucosa technique gave trouble from ascending renal infection, since that time I have used it in 16 further cases Some have been selected either because the patient was old or frail and so might withstand badly the more orthodox ureterocolic anastomosis with its occasional ileus, some were chosen because they had some impairment of renal function, and some because I now find the operation gives very satisfactory results

The operation The operation has been done in two stages (figs 22–24) In the first stage, the sigmoid colon is divided transversely some distance above the middle of the sigmoid loop, thereby ensuring that the capacity of the new "bladder" is from 400 to 500 ml , the mesosigmoid, including the marginal artery, is divided at the line of section of the gut sufficiently deep to allow the proximal end of the divided colon to be brought to the surface of the abdomen

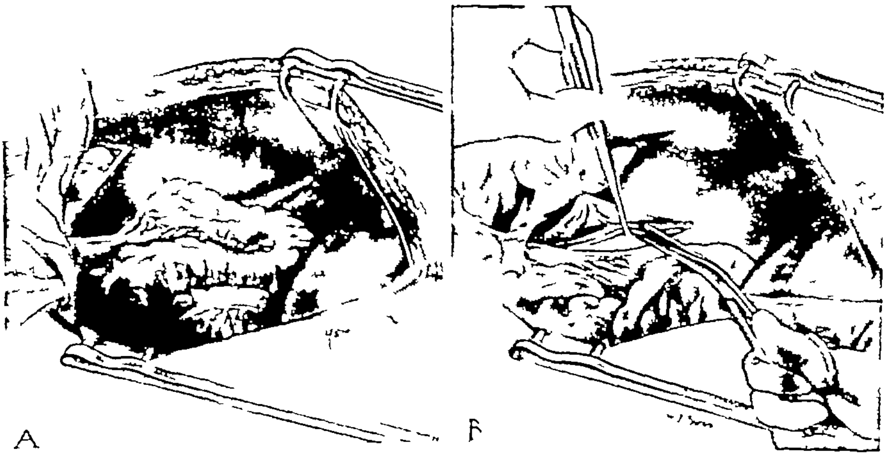


FIG 22 Operation of rectosigmoid bladder A sigmoid colon is divided transversely some distance above middle of loop mesosigmoid being divided for two to three inches Distal end of mesosigmoid infolded B, left ureter is mobilized at brim of pelvis, proximal end of divided sigmoid is brought through abdominal wall as colostomy

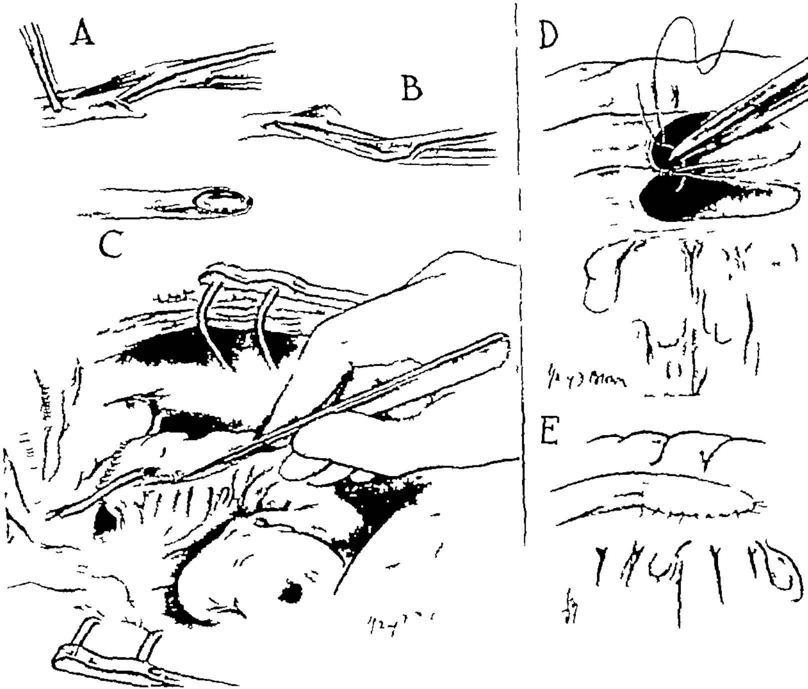


Fig 23 Operation of rectosigmoid bladder *A*, left ureter is divided and anastomosed by mucosa to mucosa technique to upper part of rectosigmoid bladder, elliptical opening is made at end of ureter *B*, two layer mucosa to mucosa ureterocolic anastomosis is made *C*, ureterocolic anastomosis completed

in the left iliac fossa without tension, through a stab-wound, as an end-colostomy, the distal end of the loop is infolded by two rows of catgut stitches The left ureter is isolated, usually at the outer side of the mesosigmoid at the level of the pelvic brim, it is ligatured low down, divided and usually transposed through a small opening in the base of the mesosigmoid to its inner side, so as to avoid kinking and is then anastomosed to the upper part of the new "bladder" In all except two cases (in which the Coffey 1, 1911, method was used), the Cordonnier (1950) direct mucosa-to-mucosa technique has been employed About fourteen days later total cystectomy is performed and the right ureter joined to the new "bladder" some distance below the left (figs 22–24)

Advantages 1) An advantage of this procedure is that it can easily be performed in two stages which adds to its safety, and the absence of an intestinal anastomosis reduces the operative risk, the postoperative course has been satisfactory and the incidence of ileus has been low

2) Because the new "bladder" does not contain feces and appears to have only a low bacterial content, the incidence of late ascending renal infection is very low, and the ureterosigmoid anastomosis can safely be done by a direct mucosa-to-mucosa anastomosis (which promotes free renal drainage), which has little tendency to late hydronephrosis and anastomotic stricture

3) I have already referred to the fact that differential electrolyte absorption takes place postoperatively in the rectosigmoid bladder, though it seems to diminish with time, but since the kidneys do not become infected it does not become a clinical problem and many patients do not take alkalies

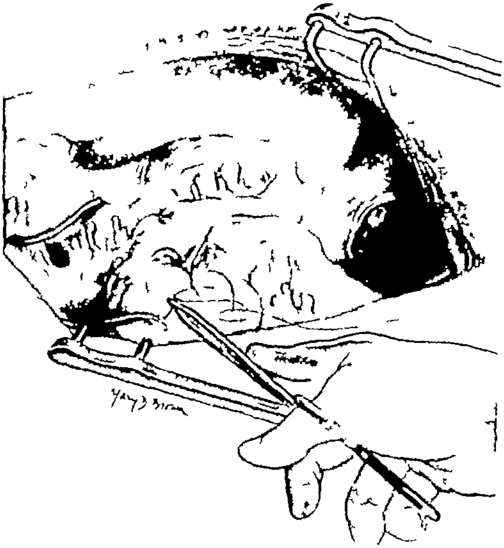


FIG 24 Operation of sigmoid bladder Ten days later bladder is removed, right ureter anastomosed to rectosigmoid

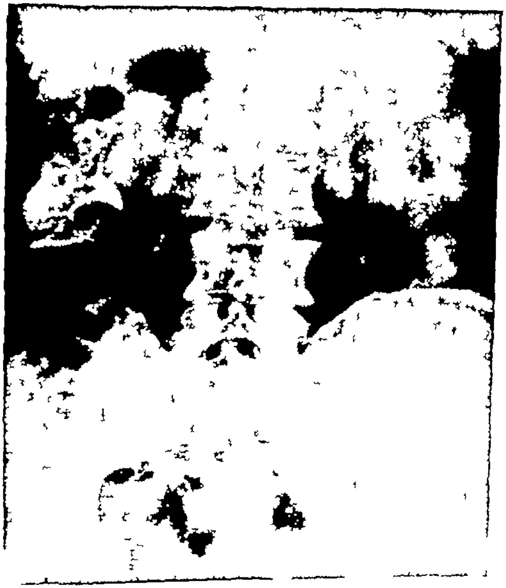


FIG 25 G A, man aged 68 Radiograph shows normal intravenous pyelogram (April 17, 1956) of patient who underwent rectosigmoid bladder and total cystectomy in 1952 No dilatation of upper urinary tract

Results Of my 20 cases, one died postoperatively from peritonitis and another on the fourteenth day from pulmonary embolism after an apparently normal convalescence Three have died from metastatic cancer, three, eighteen and twenty-four months respectively after operation, one of these had a moderate degree of hyperchloremic acidosis in the immediate postoperative period but this soon disappeared Only one case in the series, in which a temporary urinary fistula developed after the first operation has had trouble from ascending renal infection and persistent electrolyte imbalance, and after recurring attacks of infection and acidosis he finally died two years after operation with severe bilateral renal infection, which I think arose in connection with his temporary urinary fistula, all the other patients have been free from renal infection

The remaining 14 cases are alive, four for periods of between two and five years, six for periods of one to two years and four for less than twelve months after operation Only one (a very recent case) of these 14 cases has a slight hydronephrosis and this should resolve (figs 25 and 26)

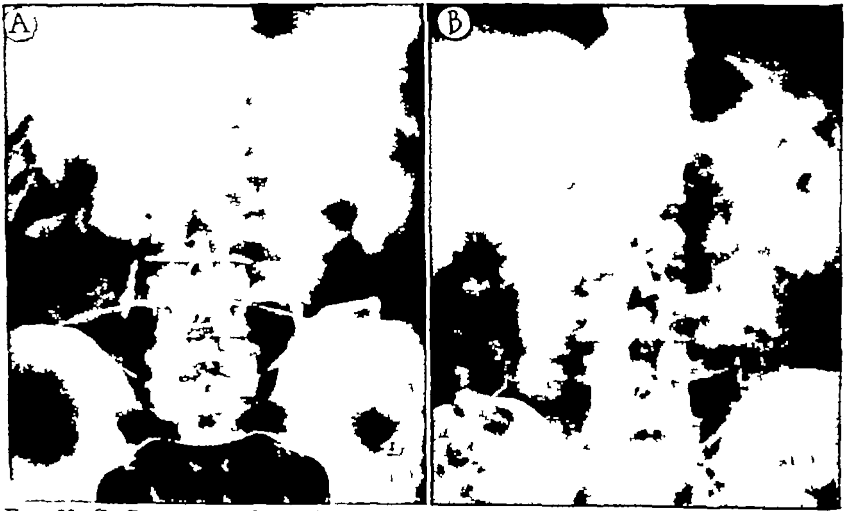


Fig 26 G S, man aged 62 *A*, preoperative intravenous pyelogram (April 8 1954), patient had cystectomy and rectosigmoid bladder in April 1954 *B*, intravenous pyelogram 10 months after operation (February 28, 1955), no dilatation of upper urinary tract

TABLE 11 *Rectosigmoid bladder Postoperative electrolyte studies Patients not taking sodium bicarbonate*

Blood electrolytes (6/15/56)

Operation	G S ♂ May 1954	T K ♂ Sept 19 2	F H ♂ Feb 1952	H R ♂ April 1956
B U N mg %	28 1	18 0	15 3	10 8
Sodium meq/L	139	130	137	135
Potassium meq/L	4 2	3 8	3 8	3 3
Chloride meq/L	102 5	102 5	102 5	104 2
CO c p meq/L	22 8	24 5	24 9	22 6

TABLE 12 *Rectosigmoid bladder with total cystectomy for cancer, 14 surviving cases*
Grade of health

Grade	Cystectomy for Cancer with Recto-Sigmoid Bladder
Grade 1	14
Grade 2	nil
Grade 3	nil
Grade 4 (failed cases)	nil
	14

Status of separate renal units
(28 renal units)

No hydronephrosis	26
Slight hydronephrosis	2
Moderate hydronephrosis	
Severe hydronephrosis	
	28

(Cordonnier anastomosis, 12 cases, Coffey 1 anastomosis, 2 cases)

Table 11 shows sample postoperative blood electrolyte readings in four patients who are not taking sodium bicarbonate, very few of the patients have, in fact, needed to take alkali and hyperchloremic acidosis has not been seen in any of the 14 survivors

Table 12 allows a comparison to be made between the grades of health and also the renal status of the 37 surviving cases with ureterocolic anastomosis previously described (table 7) and those of the 14 surviving cases with rectosigmoid bladders, every one of which have been placed in grade 1

To summarize, therefore, the results which can be obtained when ureters are transplanted into isolated intestinal segments, as compared with those obtained using the standard ureterocolic anastomosis, I would say that the late results of the patients with the rectosigmoid bladder have been appreciably better than those with the ureterocolic anastomosis in that their health has been more stable and secure, and the incidence of renal troubles has been absent in survivors and very low in the series as a whole There has been no gradation in the high quality of health of the survivors The operation, done as a two-stage procedure, is simple to perform and unassociated with much postoperative morbidity The only disadvantage is the colostomy The ileal bladder or ileal segment in association with cystectomy, while giving very good clinical results in survivors, has so far been associated with a considerable operative mortality and morbidity, as well as with a continuously draining urinary fistula, in children with spina bifida it has proved to be very satisfactory

There is much evidence, therefore, in favor of isolated rectosigmoid bladders being regarded as the most uniformly satisfactory method of urinary diversion, when associated with cystectomy

Modification of the method Some surgeons have sought to use the principles of the rectosigmoid bladder but also to render the patient more socially amenable Such an attempt was made first by Gersuny (1898) who drew the divided sigmoid downwards alongside the rectum through the anal sphincter to the perineum Lowsley and Johnson (1955) and Johnson (1956) have mobilized the upper end of the divided sigmoid colon, and brought it down in front of the rectum to emerge in the perineum in front of the anus, passing it between the muscle fibers of the anal sphincter, in order to achieve control of the feces, good results have been reported There would appear to be a risk of either stricture or prolapse of the new perineal opening if infection of the perineal wound occurs, or alternatively urinary incontinence may follow if the external sphincter is injured Further reports of this interesting procedure must be awaited

I desire to thank my colleague, Mr F P Raper, for allowing me to incorporate in the series of ileal segment cases, a number of cases upon which he had operated I also wish to thank Mr J Hainsworth and Mr A L Pegg for the photographic work, Miss M Brown for drawings of the ileocystoplasties and rectosigmoid bladders and tabular illustrations, Miss M Hart for secretarial help I am grateful to the editor of the BRITISH JOURNAL OF SURGERY for allowing me to reproduce figure 4 and to the editor of the BRITISH JOURNAL OF UROLOGY for figures 14, 18, 23

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UNILATERAL MULTICYSTIC KIDNEY IN AN INFANT

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Unilateral multiple cystic renal disease in children is of uncommon occurrence. Generally, case reports appearing in the literature have divided the disease into two categories, the multilocular variety and the so-called multicystic variety. Although most authors consider these two groups as separate clinical and pathological entities, overlapping of terminology has occurred, and reviews concerning one type may include cases of the other type and vice versa. This lack of uniformity is probably of little actual significance, since the clinical picture is similar in both types. However, of considerable importance is the tendency to classify the unilateral multicystic kidney as a variant of congenital polycystic renal disease, since this implies involvement of both kidneys. Contrary to this general belief, cases of unilateral polycystic disease have been reported as occurring in from 4 to 13 per cent of cases of congenital polycystic kidney disease by Rall and Odel[1] and in 8 per cent of the 395 cases reviewed by Bell.[2] It is noteworthy that in these reported autopsy cases of the unilateral involvement the kidneys did not differ essentially in either gross or microscopic appearance from cases of bilateral disease. This is in contradistinction to the striking difference in appearance of the unilateral multicystic kidney which characteristically consists of a conglomerate mass of varying-sized cysts which have completely replaced the kidney and are held together loosely by connective tissue. The whole mass usually has the appearance of a bunch of grapes and, as a rule, no renal tissue can be identified. Furthermore, the collecting system, namely, calyces, pelvis, and ureter, is usually absent or unidentifiable.

Probably because of its infrequent occurrence, little attention has been given this condition other than for an isolated case report in the literature. Allen[3] in his monograph mentions the multicystic kidney as being a variant of the infantile type of congenital polycystic kidney disease. He describes this variant as occurring unilaterally and differing from the usual infantile type in that the cysts vary markedly in size, in contrast to the regularly and diffusely honeycombed appearance of the bilateral type. In addition, only a few isolated islands of nephrons in varying stages of atrophy can be found, and these are separated by a stroma far more abundant than in the more usual infantile type. He also states that the ureter is frequently absent or atretic in the multicystic variety.

Frazier[4] in reviewing 31 cases of unilateral multilocular cyst of the kidney, emphasizes the basic criteria for their classification, namely, 1) there must be

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[3] Allen, A. C.: The Kidney. New York: Grune and Stratton, 1951.

[4] Frazier, T. H.: Multilocular cysts. J. Urol., 65: 351, 1951.

two or more chambers to the cyst, 2) the separating walls must be complete, and 3) the over-all arrangement is dissimilar to that of polycystic kidney disease, solitary renal cyst, and multiple cystic disease of the kidney He considers multilocular cysts as a clinical and pathological entity However, he states that the relationship between multilocular cyst, polycystic renal disease, and large solitary cysts of the kidney is not clear, and it would seem logical to assume that they may represent different manifestations of a common etiological factor, probably congenital in nature

Spence[5] in a recent review emphasizes the features of congenital unilateral multicystic kidney disease which warrant its classification as a separate entity He believes its differentiation from polycystic renal disease is particularly important because the multicystic kidney always occurs unilaterally and has a favorable prognosis, whereas in polycystic disease involvement of both kidneys is at least implied and the prognosis is ultimately fatal

It would seem evident from the foregoing discussion that the true polycystic kidney, while it may occur unilaterally, is at least morphologically similar to the bilateral disease, whereas the multicystic kidney differs significantly in appearance, and even though the etiologic factors may be the same or similar in both conditions, they should be considered as separate entities at least from a clinical viewpoint

ETIOLOGY

It is not within the scope of this paper to present a detailed discussion of the various theories pertaining to the etiology of congenital polycystic kidney disease However, the two most widely accepted theories are, first, that of Hildebrant[6] that there is malfusion between the secretory portion of the nephron derived from the renal blastoma and the collecting portion of the nephron derived from the wolffian duct, resulting in cystic dilatation due to continued secretion by the upper portion of the nephron The other theory is that of Kampmeier[7, 8] which postulated that certain early generations of the uriniferous tubules fail to atrophy as they normally do and persist to become progressively enlarging cysts

Experimental attempts to produce polycystic kidneys have been uniformly unsuccessful, with the single exception of the work of Bagg,[9] who found that a certain percentage of renal anomalies, including polycystic disease, occurred in the third and fourth generations of irradiated mice, the tendency toward congenital renal anomalies being inherited as a mendelian recessive The mechanism was unknown

CASE REPORT

M L H, No 221-236, was a full-term female infant delivered November 24, 1953, by low forceps after an uncomplicated labor On routine physical examination she was found to have an abdominal mass, approximately in the midline, that almost filled the entire lower abdomen The mass was somewhat fixed, irregular, and firm to palpation The remainder of the physical examination was entirely negative Intravenous urography revealed a normally functioning right kidney with perhaps slight dilatation of the right ureter and lateral displacement of the pelvic portion of the right ureter (fig 1) No kidney was demonstrated on the left side There was evidence of a mass in the left lower quadrant A barium enema revealed the presence of a mass with displacement of the sigmoid anteriorly and to the right Cystoscopy revealed a normal bladder for a newborn with a normally situated right ureteral orifice However, no left ureteral orifice could be found The impression at this time was that the patient had a pelvic kidney which was the cause of the mass It was uncertain whether it was a hydronephrotic kidney or whether it might be a Wilms' tumor Laboratory studies were as follows Serology, including both Kolmer and VDRL, was negative Routine urinalysis revealed a pH of 6, the quantity not being sufficient to determine specific gravity The test for albumin and sugar was negative, microscopic study revealed a few white blood cells Complete blood count disclosed 19 gm hemoglobin with 5,690,000 red blood cells, 13,150 white blood cells, 53 per cent neutrophils, 42 per cent lymphocytes, 4 per cent eosinophils, and 1 basophil The nonprotein nitrogen was 43 5 mg

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Exploration was advised as soon as the Pediatric Department felt that the child could tolerate surgery Consequently, when the child was 14 days old exploration was performed The abdomen was opened through a left pararectus incision, and on incising the peritoneum a large multicystic mass was found

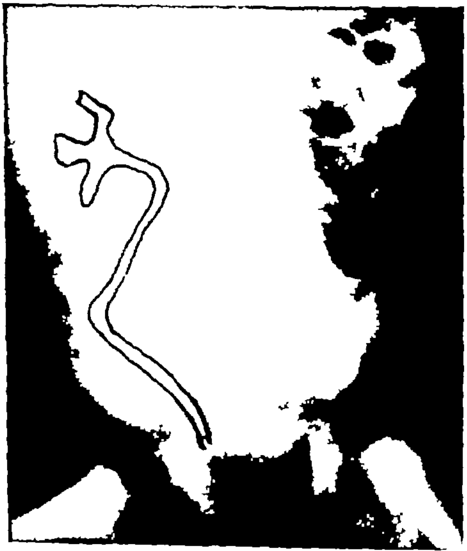

Fig 1 Excretory urogram Outline of right ureter and renal pelvis traced with ink to show slight dilatation and lateral displacement of this ureter

pushing up the posterior parietal peritoneum The mass was found to arise from the retroperitoneal space Most of the intestines were pushed to the right and upper abdomen The posterior peritoneum was incised over the cystic mass and it was removed in toto without difficulty There was a definite line of cleavage Several small groups of vessels were encountered which were clamped, cut, and tied However, no structure was identified as a renal pedicle and no structure was encountered which was thought to be the ureter The left lumbar area was explored and the patient was found not to have a kidney in this region The right kidney was palpated and felt normal although slightly enlarged

Pathological report The source of this tissue could not be recognized It consisted almost entirely of multiple, discrete, grapelike cysts which varied in size from a few millimeters to five centimeters The external covering of the cysts was smooth and glistening There was no intercommunication between the cysts and they contained within them a clear, straw colored fluid (fig 2, *A*) On cut section there was a small portion of reddish tan stroma between many of the cysts However, no recognizable renal tissue was seen There was no identifiable pelvis or ureter (fig 2, *B*) Microscopic description Approximately 20 per cent of the sections examined were composed of recognizable renal tissue which consisted of glomeruli in various stages of degeneration surrounded by a greatly dilated glomerular capsule Tubules were present, many of which were dilated and lined by a flat cuboidal type of epithelium The remaining sections were composed of varying-sized cysts lined by a flat cuboidal type of epithelium Diagnosis Polycystic kidney (fig 3)

The child had an uneventful postoperative convalescence and was discharged from the hospital on the eighteenth postoperative day Prior to discharge,

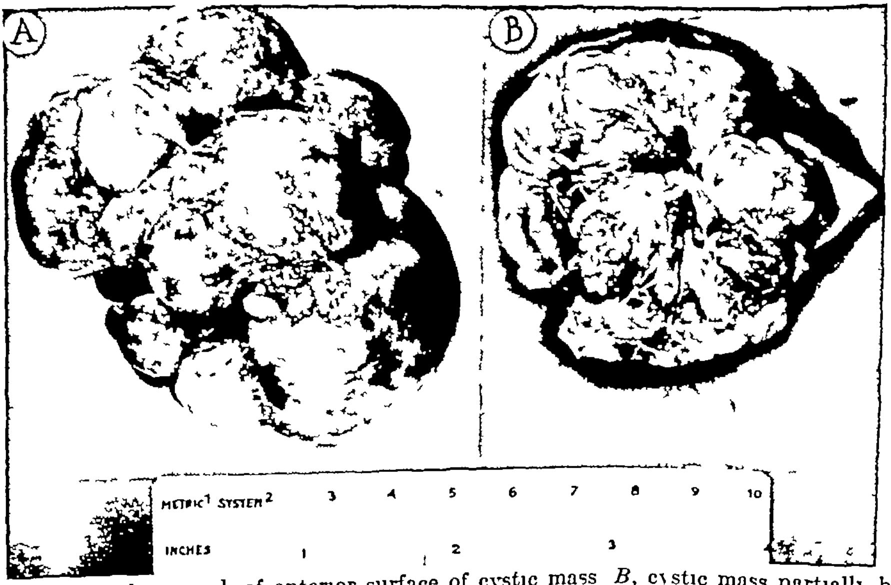

FIG 2 *A*, photograph of anterior surface of cystic mass *B*, cystic mass partially bisected to find pelvis and ureter, neither identified

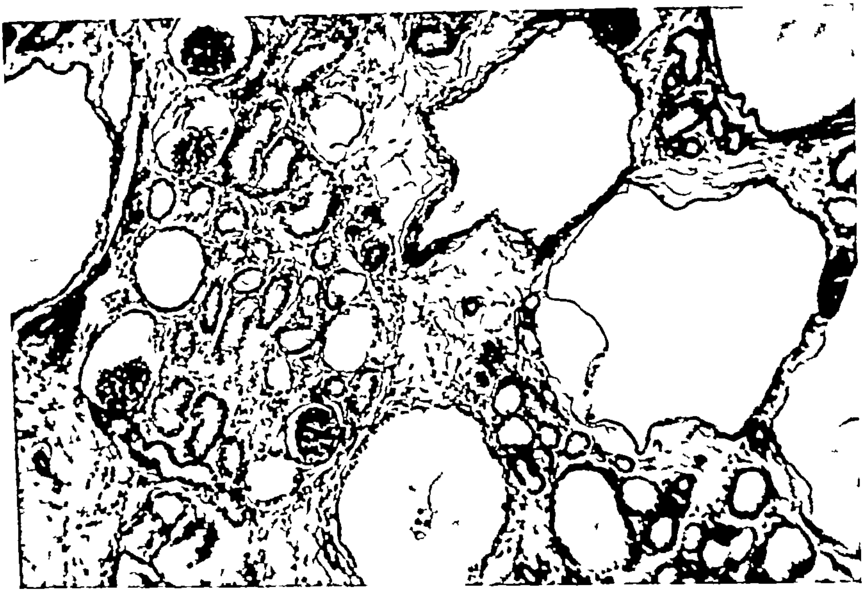

FIG 3 Photomicrograph shows cellular composition of multicystic mass

another intravenous urogram revealed that the right kidney was functioning well, no evidence of polycystic disease was apparent on this side, the ureter was no longer deviated At the time of this report the child is apparently healthy and doing well

DISCUSSION

Our case represents, we believe, a true congenital unilateral multicystic kidney Previously reported cases have been admirably reviewed by Spence,[5] and a total of 19 cases including his own were reported In addition, a case report by Lih and Waud,[10] although designated as a unilateral polycystic kidney, is typical of the type of condition under discussion and should be so classified The case herein reported would then be the twenty-first

The criteria necessary for classifying multicystic kidney disease would seem to be basically 1) unilateral involvement and 2) the typical gross appearance of the kidney The microscopic appearance is unreliable, since it may be indistinguishable from true polycystic disease

It would seem that the etiologic factor in the case presented is primary failure of the ureteral bud to develop from the wolffian duct, thus leaving the secretory elements of the renal blastoma as a series of blind tubules which progressively enlarge into varying-sized cysts This, of course, would be in agreement with the theory of Hildebrant

That this condition is congenital is obvious That it is hereditary is doubtful, since there was no family history of polycystic renal disease We have no evidence pushing up the posterior parietal peritoneum The mass was found to arise from the retroperitoneal space Most of the intestines were pushed to the right and upper abdomen The posterior peritoneum was incised over the cystic mass and it was removed in toto without difficulty There was a definite line of cleavage Several small groups of vessels were encountered which were clamped, cut, and tied However, no structure was identified as a renal pedicle and no structure was encountered which was thought to be the ureter The left lumbar area was explored and the patient was found not to have a kidney in this region The right kidney was palpated and felt normal although slightly enlarged

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Pathological report The source of this tissue could not be recognized It consisted almost entirely of multiple, discrete, grapelike cysts which varied in size from a few millimeters to five centimeters The external covering of the cysts was smooth and glistening There was no intercommunication between the cysts and they contained within them a clear, strawcolored fluid (fig 2, *A*) On cut section there was a small portion of reddish tan stroma between many of the cysts However, no recognizable renal tissue was seen There was no identifiable pelvis or ureter (fig 2, *B*) Microscopic description Approximately 20 per cent of the sections examined were composed of recognizable renal tissue which consisted of glomeruli in various stages of degeneration surrounded by a greatly dilated glomerular capsule Tubules were present, many of which were dilated and lined by a flat cuboidal type of epithelium The remaining sections were composed of varying-sized cysts lined by a flat cuboidal type of epithelium Diagnosis Polycystic kidney (fig 3)

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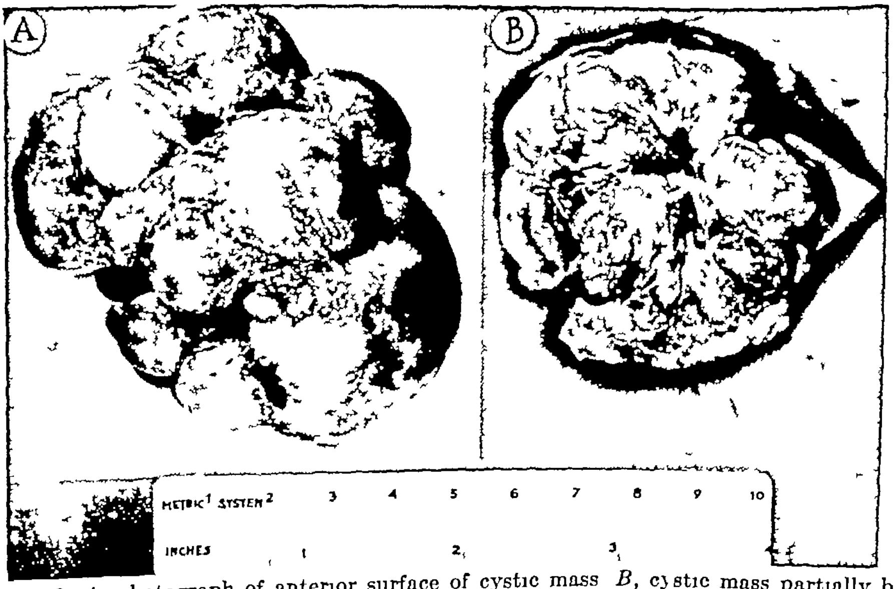
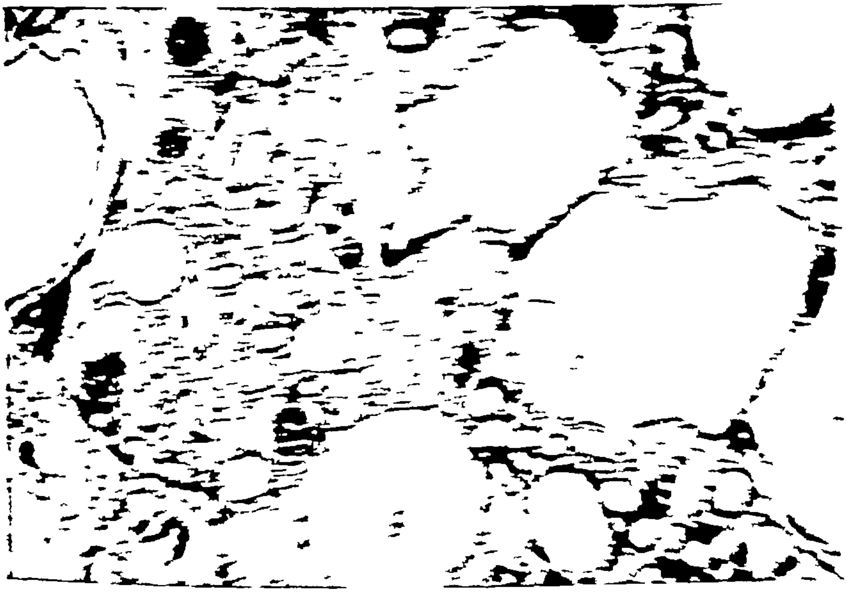


FIG 2 *A*, photograph of anterior surface of cystic mass *B*, cystic mass partially bisected to find pelvis and ureter, neither identified



as yet to assume that there is involvement of the opposite kidney, and if we may rely on previous reports there will be no such involvement

SUMMARY

Congenital unilateral multicystic renal disease is a condition in which there is replacement of the kidney by a conglomerate mass of varying-sized cysts held loosely together by connective tissue in which there is no visible renal parenchyma The ureter is frequently absent or atretic Although sometimes designated as a variant of congenital polycystic disease, the unilateral multicystic kidney should be classified as a separate entity, at least clinically, because of the unilateral involvement and favorable prognosis This is true even though the etiologic factors may be the same as those responsible for true congenital polycystic kidney disease The case presented makes the twenty-first recorded in the literature

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A METHOD OF QUICK RELIEF OF PAIN DUE TO RENAL COLIC

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The purpose of this paper is to contribute a simple method for quick relief of one of the most severe pains known, namely, renal colic. The results are so constant and gratifying that the method may be helpful to others who have faced the same problem of handling patients suffering from this condition. The standard treatment with demerol or morphine with or without atrophine requires considerable time to take effect and during that time it is also frequently impossible to obtain a good history or to do an adequate physical examination on the patient.

It is not the intention of this paper to claim originality for this method since the struggle of man against pain probably started shortly after the creation of Homo sapiens. Old and almost forgotten remedies have been rediscovered and perfected as far as the progress of science permitted at that particular time, or they have been dropped again in the dust of history.

Looking back at the history of pain control we have to go back to the most primitive tribes; for instance, in Asia and Africa one will find the most primitive forms of medicine practiced by a medicine man who usually has an extraordinary ability to combine his knowledge of herb extracts with a fair amount of psychology and a large dose of hocus-pocus. A man in the agony of renal colic turns to him for the same reasons that our patients come to us, namely for relief of his pain. The medicine man knows very well that a renal colic usually lasts a short time, but that it also may last for hours. He therefore brings forth a small statuette or fetish and after having questioned his patient about the character and location of his pain he will drive pins or nails into the corresponding site of the fetish. With prayers, magic dances, and sufficient noise to suppress the cries and lamentations of his patient, he will carry on his "treatment" until the pain subsides and everybody will go home convinced of the magic healing powers of this great medicine man. In the next step of the evolution of medicine, the pins are not inserted in the fetish but in the skin of the patient, followed usually by the same or similar rites. A widespread cure for ailments as pneumonia, abdominal pains, and colics is cauterization of the skin over the area where the pain is felt. In Saudi Arabia for instance I have seen this done by contact with the heated head of a large nail, in remote areas of Canada electric cauterizers are used. This treatment is so effective that magic dances are no longer necessary. These methods I am sure will be met by the physicians of this era with a smile, but it is wise not to push aside the knowledge of the primitive people because essential drugs such as opium, digitalis, curare, etc. were long used by people before their occurrence in our pharmacopoeia.

It is a well noted fact that visceral organs can be handled and cut, crushed or burned without causing any pain as long as traction on the mesentery or

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stimulation of the abdominal wall is avoided Indeed, viscera are sparsely innervated Kinsella has shown that the viscera are definitely sensitive if adequate stimulus is applied, and the threshold of pain fibers may have been lowered by the pathological state The adequate stimuli for visceral afferents are those arising from their own environment and especially from their own activities and pathological state For instance, 1) spasms or strong contractions especially when accompanied by ischemia, 2) sudden distention against resistance, 3) chemical irritants, 4) mechanical stimulation, especially when the organ is hyperemic While the organic sensations and visceral reflexes are served by afferents in the parasympathetic nerves, the impulses serving visceral pain are conducted in the sympathetic nerves, except for the viscera in the pelvic region, the esophagus and trachea Impulses arising in visceral structures give rise to pain frequently localized in superficial structures at a considerable distance from the disturbed organ Such pain is known as referred pain The referred pain follows the dermatomal rule, namely, it is referred to the dermatomes supplied by the posterior roots through which the visceral afferent impulses reach the spinal cord Visceral irritation by pathological process may be manifested in a) pain or b) hyperalgesia, hyperesthesia, or tenderness c) autonomic reflexes and d) somatic reflexes The first two manifestations are of most interest to us in this particular pathological condition

An explanation of this referred pain is that some visceral afferents converge with cutaneous pain afferents to end upon the same neuron at some point in the sensory spinothalamic or cortical pathway and these systems of fibers are organized in such a manner that the dermatomal reference is provided The impulses coming from the spino-thalamic tract are interpreted by the brain as coming from the skin To say it in the words of Wolff and Hardy as they describe it in their article "On the Nature of Pain" "Referred pain may be accentuated in intensity by virtue of effects of ordinarily non-noxious stimuli from

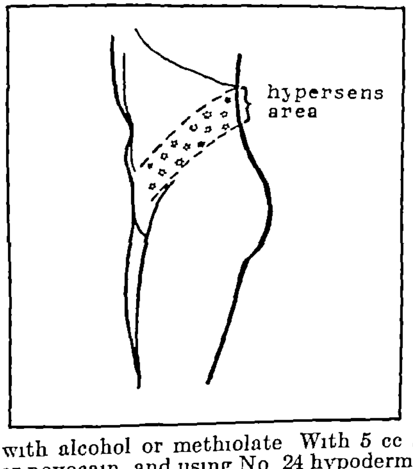

FIG 1 Skin cleansed with alcohol or methiolate With 5 cc syringe filled with 1 per cent solution of procaine or novocain, and using No 24 hypodermic needle, multiple intracutaneous injections of approximately one- or two tenths of cubic centimeter are given (*) Injections are evenly spaced in hypersensitive area, but pattern is not important

zones of reference Impulses from such sources normally inadequate to produce pain may do so upon reaching the cord in a segment involved in central spread of excitation '

McClellan and Goodell experimenting with the ureter of a female patient by faradic stimulation of the ureter high up near the kidney found the pain referred along the border of the rectus muscle approximately at the level of the umbilicus This pain disappeared quickly and was followed in half an hour by a dull ache in the flank This ache increased gradually and lasted six hours Most of the pain was found in the costovertebral angle The tenderness of the back muscles most likely was due to skeletal muscle contraction In acute appendicitis in the early stage there is a similar area of pain around the umbilicus which later on shifts down to McBurney's point There is a definite area of hypersensitivity which can be demonstrated by scratching a pin over the skin An ice bag applied to the skin of the right lower quadrant will reduce pain

In renal colic we have an area of hyperesthesia in the flank running from the costovertebral angle down to the groin This area can easily be located by scratching the skin with a pin or needle and subsequently marking the area with ink Multiple intracutaneous injections of a tenth of a cc of a 1 per cent procaine solution in this hypersensitive area (fig 1) produce instant disappearance of the sharp colicky pain Patients who are rolling and tossing in agony, suddenly become quiet and relaxed There remains a dull ache which is very mild in comparison with the previous acute pain and is comparable to the soreness of muscle spasm

It is now possible to examine the patient properly One can make him lie still on the x-ray table holding his breath while the pictures are taken

The spasm originating in the ureter or the pelvis around the irritating stone is not now felt by the patient Antispasmodics can be given to relieve the spasm of the ureter and further conservative treatment or surgical intervention naturally follows This very interesting subject of referred pain is still wide open for scientific research, but it was believed that the results of this method of treatment were dramatic enough to justify its presentation to the profession

SUMMARY

A simple method for quick pain relief in renal colic has been described The mechanism of referred pain with superficial and or deep hyperalgesia has been discussed briefly

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TABLE 1

Pyeloureteroneostomy without a ureteral splint, group 1

	Hydronephrosis	Gross bone	Microscopic bone
1 Dog No 975 Nephrectomy 1 week post anastomosis	No (but dilated)	No	No
1 Dog No 548 Nephrectomy 2 weeks post anastomosis	Obliteration of anastomosis	No	Yes
1 Dog No 444 Nephrectomy 3 weeks post anastomosis	Yes	Yes	Yes
1 Dog No 861 Nephrectomy 5 weeks post anastomosis	Yes	Yes	Yes
1 Dog No 397 Nephrectomy 7 weeks post anastomosis	Yes	Yes	Yes
1 Dog No 416 Nephrectomy 7 weeks post anastomosis	Yes	Yes	Yes
1 Dog No 654 Nephrectomy 9 weeks post anastomosis	Yes	Yes	Yes
1 Dog No 907 Nephrectomy 32 weeks post anastomosis	Yes	Yes	Yes
8 Total			

Pyeloureteroneostomy with a polyethylene splint, group 2

	Hydronephrosis	Gross bone	Microscopic bone
1 Dog No 515 Nephrectomy 2 weeks post anastomosis	No	No	Yes
1 Dog No 579 Nephrectomy 3 weeks post anastomosis	No	No	Yes
1 Dog No 588 Nephrectomy 4 weeks post anastomosis	No	No	Yes
1 Dog No 598 Nephrectomy 5 weeks post anastomosis	Giant hydro (splint came out)	No	Yes
1 Dog No 561 Nephrectomy 7 weeks post anastomosis	Giant hydro bone formed at site of splint	Yes	Yes
1 Dog No 586 Nephrectomy 7 weeks post anastomosis	No	No	Yes
1 Dog No 523 Nephrectomy 9 weeks post anastomosis	No	No	Yes
1 Dog No 651 Nephrectomy 25 weeks post anastomosis	Yes	No bone in pelvis solid bone in upper ureter 1 cm long by $\frac{1}{2}$ cm diam lumen 1 mm	Yes
8 Total			

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BONE FORMATION IN EXPERIMENTAL PYELOURETERONEOSTOMY

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This series of experiments attempting to reproduce and clarify the process of extraskeletal ossification was conceived while we were devising a procedure for ureteropelvic reimplantation The anastomosis of an accidentally evulsed ureter from an intrarenal pelvis may be extremely difficult or even impossible The operation which was performed resulted in the formation of bone at the site of the ureteropelvic anastomosis This unexpected finding led to a review of the literature and to the experiments reported here

PROCEDURE

Sixteen mongrel dogs were used The right kidney in each animal was exposed through a subcostal incision The ureter was freed from the surrounding areolar tissue and divided at the ureteropelvic juncture The renal pedicle was skeletonized and a soft-shod Blalock clamp was placed across the pedicle to compress it The kidney was then split from pole to pole along Brödel's line In this manner, the calyces and pelvis of the kidney were opened and the ureter, which had been divided at the ureteropelvic juncture, was brought up into the pelvis of the kidney The pelvis of the kidneys in dogs is usually intrarenal The proximal centimeter of the severed ureter was divided longitudinally These two flaps were secured to the intrarenal pelvis using interrupted fine catgut sutures Nephrostomy tube drainage was not used in any of these animals, and no attempt was made to secure bleeding points in the renal parenchyma The first few animals promptly acquired hydronephrosis due to obstruction at the site of the reimplantation A polyethylene tubing was then used to splint the anastomosis in eight of the animals This tubing was sutured to the pelvis of the kidney and was placed in the distal ureter, thus bridging the anastomosis Before loosening the clamp on the renal pedicle, the kidney was closed with interrupted mattress sutures of No 00 chromic catgut on an atraumatic intestinal needle These sutures were placed over strips of ribbon gut fixed to the edges of the divided kidney The ribbon catgut was used to prevent the mattress sutures from cutting through the parenchyma The capsule was closed with a continuous suture of No 00 atraumatic chromic catgut

The clamp on the renal pedicle was left in position throughout the plastic reconstruction of the pelvis and the closure of the kidney This procedure required from 30–40 minutes After the clamp had been removed the flank incision

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Pyeloureteroneostomy with a polyethylene splint, group 2

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1 Dog No 579 Nephrectomy 3 weeks post anastomosis	No	No	Yes
1 Dog No 588 Nephrectomy 4 weeks post anastomosis	No	No	Yes
1 Dog No 598 Nephrectomy 5 weeks post anastomosis	Giant hydro (splint came out)	No	Yes
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8 Total			

was closed in layers with one Penrose drain which was brought out through the superior aspect of the wound

At intervals of 1, 2, 3, 5, 6, 9, 25, and 32 weeks after the operation, nephrectomies were performed on all 16 dogs The site of anastomosis was examined for grossly discernible bone, and sections for microscopic examination were taken through the anastomosis and kidney parenchyma An x-ray film was made of one of the kidneys which contained bone

RESULTS

Table 1 summarizes the results obtained in the 16 dogs The eight dogs in group 1 had pyeloureteroneostomy without ureteral splinting The first dog, No 975, had a nephrectomy one week after the anastomosis and no gross or microscopic bone was found Dog No 548, which had no ureteral splint, and dog No 515, which had a splint, were both examined two weeks postoperatively At that time, both animals showed microscopic but not gross bone at the site of the anastomosis Of the eight animals in the first group which were reoperated upon at various times after the second week, six had hydronephrosis and gross and micro-

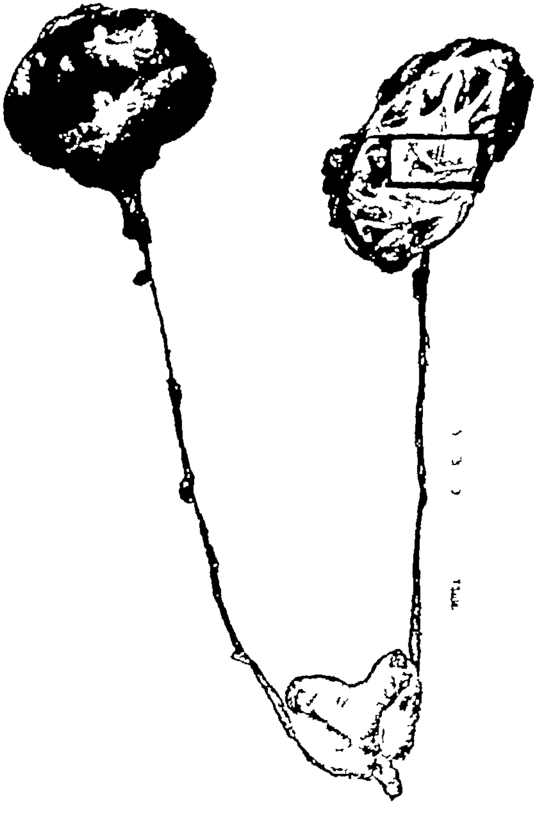

FIG 1 Dog No 907 Thirty two weeks after pyeloureterostomy Plates of bone are prominent beneath both flaps of ureter at the site of anastomosis See figure 4, *B*

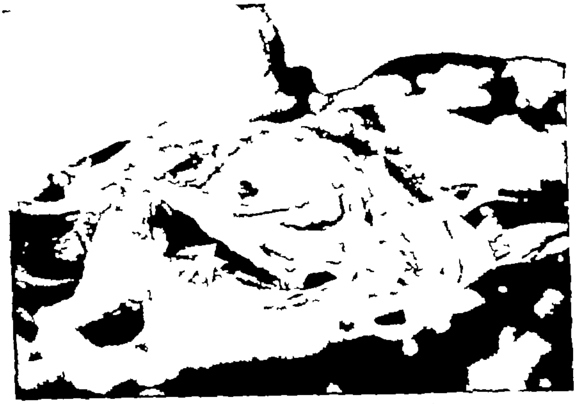

Fig 2 Enlargement of outlined area

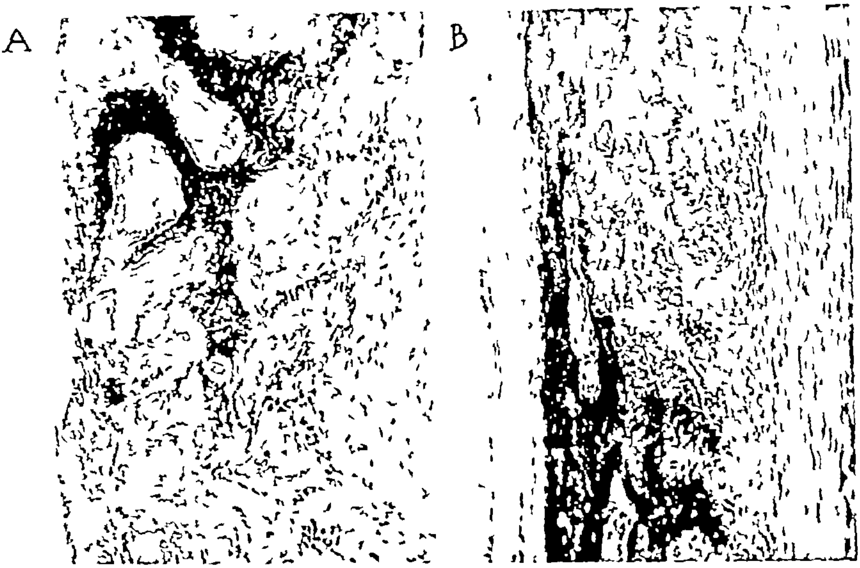

Fig 3 A dog No 548 Two weeks after pyeloureterostomy Calcified new bone has formed immediately beneath pelvic mucosa More newly formed osteoid surrounded by rows of astroblasts makes up more distant spicules Everywhere there is active fibroblastic proliferation H & E × 115

B dog No 444 Three weeks after pyeloureterostomy Continuous layer of bone lies beneath mucosa It is thicker and contains less osteoid than at two weeks, but is still actively growing There is much inflammation H & E × 90

scopic bone formation Six of the eight dogs in which a splint was used, group 2, did not acquire hydronephrosis nor was gross bone found in these animals However, microscopic bone was found in all dogs in this group

Figure 1 is a photograph of both kidneys and the bladder of dog No 907 It illustrates the replacement of submucosal tissue by bone in both flaps of the ureter A probe is in the ureter Figure 2 is an enlargement of the area within the black lines in figure 1 The arrow points to the spicule of bone

SUMMARY OF MICROSCOPIC FINDINGS

In less than two weeks after the operation, bone was formed at the site of the ureteropelvic anastomosis The greater amount of bone appeared to be laid down beneath the ureteral mucosa rather than beneath the pelvic mucosa The bone formation began just beneath the epithelium The first change to occur in the area of anastomosis was a rapid proliferation of fibroblasts in the subepithelial region These cells were large and had basophilic cytoplasm which apparently took on osteoblastic activity They were always associated with the newly formed bone, and by the time they had disappeared, the growth of the bone had ceased The bone formation extended longitudinally beneath the mucosal surface, and by nine weeks might be 2 cm or more in length By 32 weeks it had not progressed any further In the early stages, the formation of bone was active In the later stages, there was some resorption However, even at nine weeks, active bone formation could still be demonstrated along with the resorption

The rapidity with which the formation of bone took place varied directly with the amount of damage to the kidney In those kidneys in which hydronephrosis and infection occurred, the bone appeared earlier and grew more rapidly However, even in those dogs in which the anastomosis was protected by the polyethylene splint some bone was formed even though there was no evidence of hydronephrosis and consequent infection After a period of seven weeks bone formation became as extensive as it was in the hydronephrotic kidneys

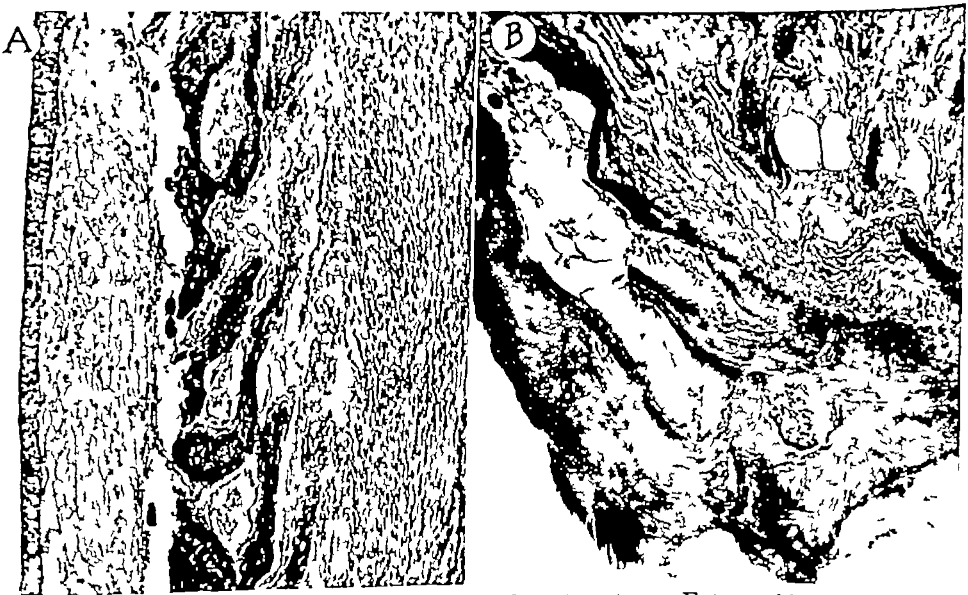

Fig 4 *A*, dog No 397 Seven weeks after pyeloureterostomy Extent of bone is greater than at three weeks, but absorption has begun on mucosal side as evidenced by lacunae and giant osteoclasts Peripherally there is osteoid and continuing osteoblastic activity H & E × 100

B, dog No 907 Dense trabeculae of bone are quite inactive save for scattered astro clasts, indicating some resorption Marrow spaces containing both hematopoietic tissue and fat have formed H & E × 115

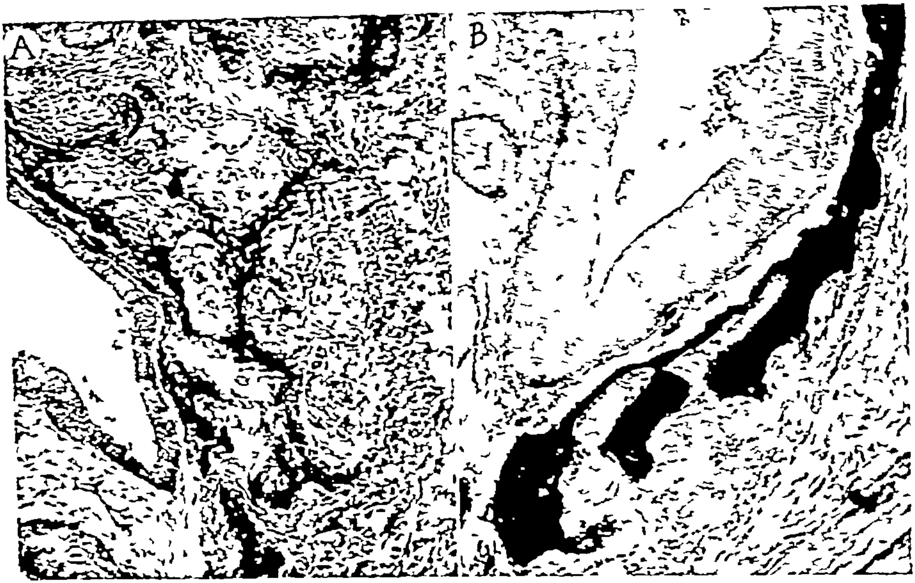

Fig 5 *A*, dog No 515 Two weeks after pyeloureterostomy with splint Trabeculae of osteoid and partially calcified new bone lie in cellular inflamed fibroblastic tissue beneath mucosa of anastomosis Bone formation is more advanced in vicinity of epithelium lining the pelvis H & E × 115

B, dog No 586 Seven weeks after pyeloureterostomy with splint Calcified mature bone is extensive on epithelial side but absorption has begun here, while on distal side osteoblasts are active and osteoid is being formed H & E × 115

The proximity of the bone to the epithelial layers of the mucosa suggested that bone formation might in part be the result of diffusion of material in the retained and often infected urine in the pelvis into the surrounding pelvic tissues Once the formation of bone started, it tended to continue by extending into the peripelvic connective tissue away from the mucosal surface When resorption was observed, it was in the older bone immediately adjacent to the mucosal epithelium

Figures 3 through 5 are photomicrographs showing the amount and structure of the bone at various periods after pyeloureteroneostomy

DISCUSSION

Many investigators have noted the development of bone in the urinary tract of animals Litton (quoted by Kossa),[1] in 1880, appears to have been the first to report the production of bone by undifferentiated fibroblasts He experimented on rabbits and was able to produce bone in their kidneys by ligating the vascular pedicle Sacerdotti and Frattin[2] reported the results of their experiments in 1901 These experimenters concluded "While from these studies it is evident that bone is formed first by metaplasia of the connective tissue and later by osteoblastic apposition, the formation of bone marrow cannot be explained but one can theorize that this happens because normally the process of ossification is always

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[1] Litton Quoted by Kossa [1]

[2] Sacerdotti C and Frattin G On the heteroplastic production of bone Giornale della R Accademia di Torino Anno LXIV series 4 vol 7 Translated by Dr Giuseppe Petruzzelli

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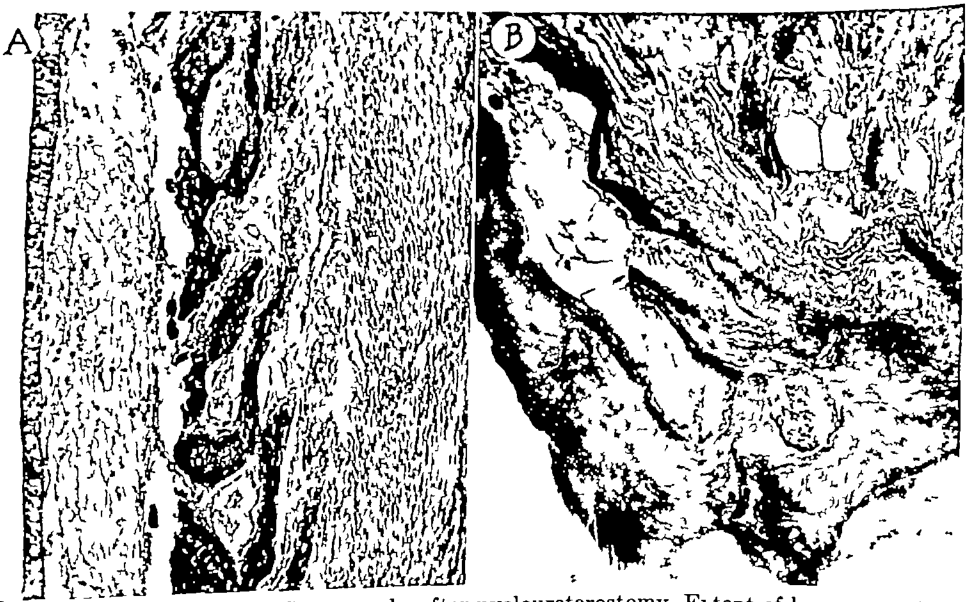

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CLINICAL IMPLICATIONS

It is interesting to speculate on the possible therapeutic value of the development of extraskeletal bone If bone could be produced with an adequate amount of marrow, it is conceivable that it might be useful in the treatment of certain anemias It is also interesting to think of the possibility of growing tissue cultures of fibroblasts from the area in which we have been able to produce bone If they will continue to change from fibroblasts to osteoblasts in tissue culture the usefulness of this material in the treatment of ununited fractures and in various plastic procedures would be tremendous

SUMMARY AND CONCLUSION

Osteoid and bone were formed at the site of surgical anastomosis of a previously severed ureter and renal pelvis in fifteen of sixteen dogs

The rapidity with which the formation of bone took place varied directly with the amount of inflammation and the degree of hydronephrosis

The extraskeletal ossification resulted from a metaplasia of newly formed fibroblasts into osteoblasts This phenomenon remains unexplained and will be the subject of further investigation accompanied by production of bone marrow, or that these cells could come from transformation of the connective tissue " The present studies reach much the same conclusion Kossa[3] also noted the formation of bone in the kidneys of rabbits which had had their renal arteries ligated It is of interest that some of the early investigators noted calcification in the rabbit kidneys We found only one or two examples of the deposition of calcium in the tubules of the dogs' kidneys R M Pearce[4] in 1909 noted the development of bone in the pelvis of dogs' kidneys which were partially resected in an attempt to study the regeneration of normal renal parenchyma He observed the development of bone from the connective tissue Pearce also noted that the bone always formed in the tissue immediately beneath the mucosa of the pelvis and usually in the angle or in the lower portion of the pelvis near the origin of the ureter The proximity of the bone to the mucosa is striking in our experiments as well Straus[5] noted the formation of bone during his attempts to produce an artificial ureter from the abdominal wall In 1917 Neuhof[6] observed the formation of bone in bladders where strips of fascia lata were used to repair defects in the bladder wall Asami and Dock[7] in 1920 again noted the formation and reabsorption of bone in the kidneys of rabbits Huggins, in 1931[8] and 1939[9] and Abbott, Goodwin, and Stephenson[10] demonstrated on dogs that when tissue from the urinary tract was transplanted to rectus sheath, fascia lata, muscle, subcutaneous tissue, and mucous membrane, bone was formed These animals developed true spongy bone with haversian canals Extraskeletal bone formation following operations on the urinary tract in man has been reported numerous times Sewell, Siceluff, and Horton[11] in 1949 reported a case of extraskeletal bone formation following suprapubic prostatectomy Klinger[12] described the spontaneous formation of bone in the middle third of the human ureter This bone consisted of trabeculae with fat and marrow filling in the spaces Tedeschi and Holtham[13] summarized much of the early work in their report on renal ossification

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[3] Kossa, J V Experimental calcification in the organism Beitrage zur path anat , **29** 160–203, 1901

[4] Pearce, R M Notes on the later stages of the repair of kidney tissue (dogs) with special reference to proliferation of the pelvic epithelium and heteroplastic bone formation J Med Res , **20** 53–65, 1909

[5] Strauss, A A Artificial ureter made from abdominal wall Surg , Gynec & Obst , **18** 78–84, 1914

[6] Neuhof, H *Fascia transplantation into visceral defects* Surg , *Gynec & Obst* , **24** 383–427, 1917

[7] Asami, A and Dock, W Experimental studies on heteroplastic bone formation J Exp Med , **32** 745–765, 1920

[8] Huggins, C B The formation of bone under the influence of epithelium of the urinary tract Arch Surg , **2** 377–408, 1931

[9] Huggins, C B Bone and calculi in the collecting tubules of the kidney Arch Surg , **27** 203–213, 1933

[10] Abbott, A C , Goodwin, A M and Stephenson, E Heterotopic bone formation produced by epithelial transplants from urogenital tract of dogs, rabbits, guinea pigs and cats J Urol , **40** 294–311, 1938

[11] Sewell, W S , Siceluff, J G and Horton, J D Extraskeletal bone formation following suprapubic prostatectomy Case report J Urol , **62** 842–844, 1949

[12] Klinger, M E Bone formation in the ureter A case report J Urol , **75** 793–795, 1956

[13] Tedeschi, C G and Holtham, W H Renal ossification Report of occurrence in aplastic kidney J Urol , **68** 50–59, 1952

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The patient was treated as a case of subacute glomerulonephritis, with bed rest, controlled diet, reserpine, 25 mg per day, and oral penicillin, 200,000 units per day At the end of five weeks, although the hypertension was unchanged, his

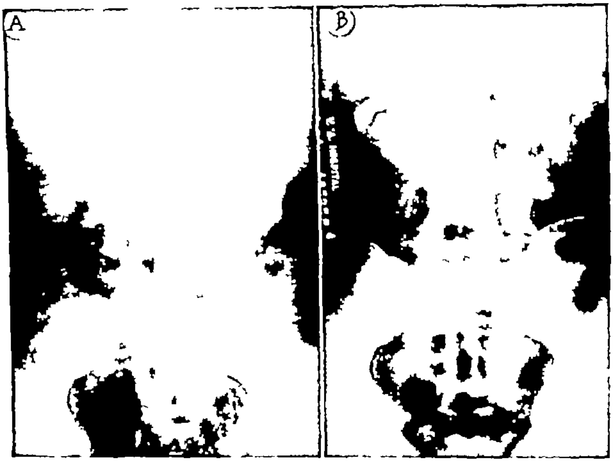

FIG 1 *A*, intravenous pyelogram following five weeks' medical treatment and as soon as blood nonprotein nitrogen approached normal levels Little or no excretion from right kidney, fair to good excretion from left with dilatation of pelvis, calyces and upper ureter *B*, retrograde pyelogram, four days after intravenous pyelogram, shows symmetrical dilatation of pelves and upper ureters Although both ureters are sharply angulated, note dilatation below as well as above angulation

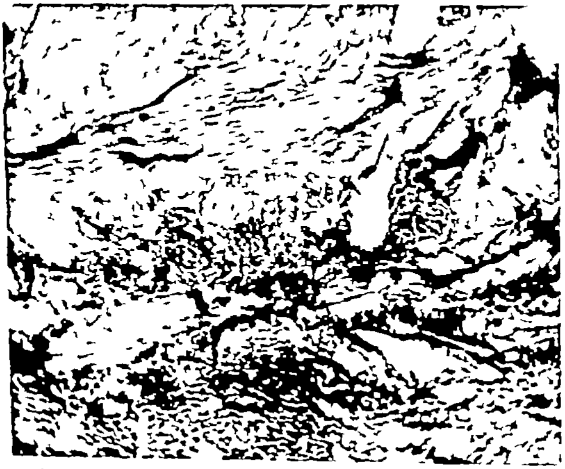

FIG 2 Section from biopsy of ureteral wall Smooth muscle cells with adjacent collagenous fibrous tissue through which are scattered chronic inflammatory cells, occasionally surrounding small fatty vacuoles

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OBSTRUCTION OF BOTH URETERS BY RETROPERITONEAL INFLAMMATION

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An inflammatory retroperitoneal process with distinct histological characteristics has recently been described by a number of observers as a cause of bilateral ureteral obstruction with subsequent renal failure In the 16 reported cases, the pathological findings and clinical manifestations have been similar A seventeenth case is now added, and, with the co-operation of the earlier authors, followup reports are included on 14 of the previous 16 It is possible from these data to draw some tentative inferences as to the natural history of this process, its pathology, and the most appropriate approach to treatment The etiology is obscure, but therapy directed at ensuring adequate drainage and controlling infection can reverse a course which may otherwise be fatal

CASE REPORT

A man aged 40 was admitted to the medical service of the hospital complaining of anorexia, evening oral temperatures of 99F, a 10-pound weight loss, progressive incapacitating fatigue, and bilateral intermittent lumbar and flank pain of six months' duration Nocturia and diurnal frequency had developed during the previous two months A severe sore throat, which had spontaneously resolved without antibiotic therapy, preceded the onset of symptoms by three months A urinalysis two months prior to admission revealed red blood cells, albumin and white blood cells A more recent examination revealed only red blood cells The past history included no serious illnesses, and the only previous hospitalization had been for a tonsillectomy

Physical examination showed a chronically ill, well developed, slender white man with temperature of 98 6F and blood pressure of 190/110 in each arm The eyegrounds were not remarkable, a grade 1 systolic apical murmur was present No abdominal masses were present, and no tenderness in the costovertebral angles

Laboratory data Hemoglobin, 11 6 gm /100 ml , white blood cell count, 11,300/cu mm with 65% neutrophils, sedimentation rate, 36 mm/hr, blood nonprotein nitrogen, 94 mg % , blood sodium, 140 meq/L, blood potassium, 5 2 meq/L, blood chloride, 103 meq/L, blood CO_2 , 18 5 meq/L, blood cholesterol, 278 mg % , blood calcium, 12 3 mg %, blood phosphorus, 6 7 mg % , serum total protein, 7 7 gm % , serum albumin, 5 1 gm % , serum globulin, 2 6 gm %

Urinalysis showed five red blood cells and three white blood cells per high power field in a centrifuged specimen Phenolsulfonphthalein excretion totaled 18 per cent in 30 minutes and 26 per cent in 2 hours A Kepler water test revealed specific

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Read at annual meeting of American Urological Association, Pittsburgh, Pa , May 6–9, 1957

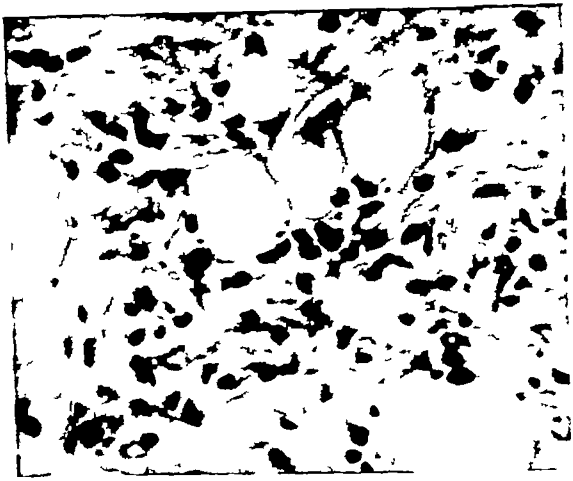

FIG 4 High power field from figure 3, *B*

Six weeks after admission, exploration of the right side revealed a mass of dense fibrous tissue enveloping the ureter from the level of the top of the fourth lumbar vertebra to just below the crossing of the iliac vessels which were also surrounded When this was peeled away, the ureter appeared relatively normal, except for a 3 cm segment of fusiform thickening of its wall There was no evidence of intraperitoneal inflammation A T tube was placed in the middle third of the ureter, and the thickened portion covered by normal fat swung from beyond the fibrotic area Biopsy (fig 2) of the ureteral wall was reported, "Smooth muscle cells with adjacent collagenous fibrous tissue, through which are scattered chronic inflammatory cells occasionally surrounding small fatty vacuoles" The retroperitoneal tissue showed cyst-like fatty spaces of varying size incorporated in dense fibrous tissue (figs 3 and 4) Swab culture from the biopsy site of the retroperitoneal tissue was sterile

The postoperative course was uneventful until the tenth day when low-grade fever developed on the fourteenth day, the T tube was removed, the impression being that it was impeding rather than facilitating drainage two days later the temperature rose to higher levels and retrograde ureterogram showed extravasation, apparently at the site of the biopsy A nephrostomy was done, and was followed by antibiotic therapy with penicillin and streptomycin for 9 days Pseudomonas aeruginosa was cultivated from the urine sensitive to furadantin, and this drug was employed for 6 days more The fifteenth day after nephrostomy excretory urography showed good function bilaterally with a normal tract demonstrated on the left (fig 5, A) Medication was discontinued and 10 days later the excretory urogram demonstrated recurrence of left hydronephrosis (fig 5 B) The nephrostomy tube was removed, and furadantin therapy reinstituted Eleven days later the excretory urogram revealed regression of the left hydronephrosis the right kidney showed fair function and seemed to drain well (fig 5, C The medication was continued for a month it has not been re-general condition had improved and the nonprotein nitrogen had fallen fro 94 to 25 mg per cent An excretory urogram was done because intermitten costovertebral angle tenderness had been observed The right kidney showed little or no excretion of the medium, the left showed fair excretion with dilatation of the pelvis and the upper third of the ureter (fig 1, *A*) On cystoscopic examination, the bladder, trigone, ureteral orifices, and vesical neck were normal Efflux from the right ureteral orifice contained indigo carmine in poor concentration 14 minutes after intravenous injection, on the left side, the dye appeared in fair concentration after four minutes Size 6 ureteral catheters were passed up both ureters without meeting obstruction Retrograde pyelograms showed symmetrical dilatation of both pelves and upper ureters (fig 1 *B*) Cultures rom both kidneys taken at this time were sterile

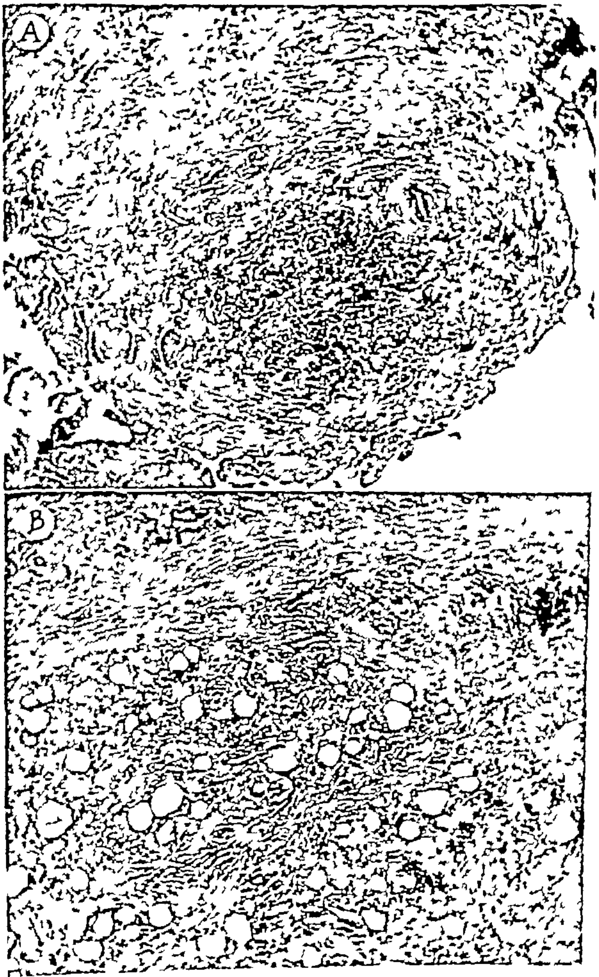

Fig 3 *A*, section from biopsy of retroperitoneal tissue (low power) shows granulomatous appearance *B*, another low power section shows cyst like fatty spaces

30 minutes 78 per cent in 2 hours Blood pressures taken daily ranged from 103 to 132 over 84

Since discharge the patient has been asymptomatic gained 30 pounds and is working daily as a school teacher A year after his admission the urine remains negative

DISCUSSION

Of the 16 previously reported cases followup data are available to 1956 on 13 and to 1954 on one Three of these 14 are now dead The other 11 and the present case were living and well as of October 1956 Of the entire series 11 were males and six females the ages ranged from 23 to 64 years 11 were between 40 and 45

Symptomatology

The onset and development of the process are so insidious that on admission renal failure was present or imminent in all but two of the patients [2] The duration of symptoms prior to hospitalization was from 10 days to two years in nine of the 15 for whom this was recorded it was three months or longer One patient had a laminectomy [3] and one a hysterectomy in consequence of these symptoms Pain usually dull was present in 16 of the 17 cases in seven it was unilateral and in nine bilateral usually involving the flank loin or abdomen The urinary output was affected in nine patients more than half of the series Of these seven had anuria and two oliguria Impotence was a symptom in one fatigue, nausea anorexia and weight loss were common probably from the developing uremia

Etiology

Reviews of histories and studies during hospitalization have failed to demonstrate the etiology of this process A number of antecedent illnesses and operations were described but none common to two or more patients except appendectomy which had been done in three of whom two had had a cholecystectomy at the same time One of these three had also had bacillary dysentery Another patient in the series had had ulcerative colitis for nine years Considering the nature of the process, it would appear reasonable to seek out a background of infection that might somehow have reached the retroperitoneal space but no better evidence than this can so far be offered

The history of previous genitourinary tract disease was uniformly negative in all but one patient in whom Pseudomonas aeruginosa and Escherichia coli infection had been demonstrated [5] Special studies were done on various patients

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[illegible] F O Bilateral ureteral obstruction due to envelopment and compression by an inflammatory retroperitoneal process J Urol 69 [illegible]

[illegible] J H and [illegible] M A Bilateral [illegible] J Urol 76 [illegible]

[illegible] J K Bilateral ureteral obstruction due to envelopment and compression by an inflammatory retroperitoneal process J Urol 59 [illegible]

[illegible] B [illegible] 45 [illegible]

[illegible] J A [illegible] B [illegible] J Urol 72 [illegible]

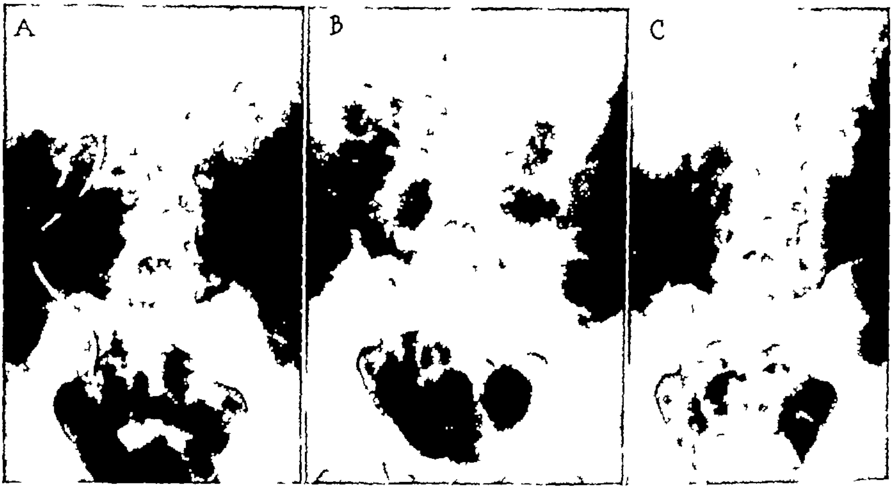

FIG 5 Excretory urograms *A*, 15 days after right nephrostomy, followed by antibiotic therapy Left kidney, which has not been operated upon, appears almost normal (Compare with figure 1 *A*) *B* 10 days after that shown in *A*, after antibiotic therapy had been discontinued Left kidney again appears hydronephrotic *C*, 11 days after figure 5, *B* (Patient had been taking furadantin during interval) Left hydronephrosis has again regressed Right kidney shows fairly good function and seems to be draining reasonably well

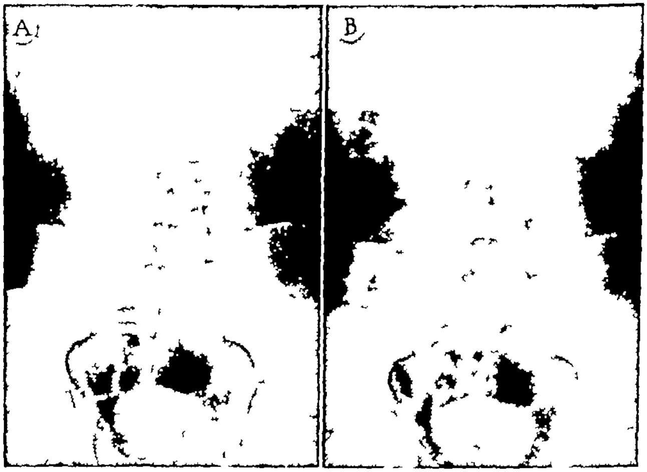

FIG 6 Excretory urograms *A*, taken little more than year after admission to hospital Right kidney shows some distortion and caliectasis, but function seems good and no gross hydronephrosis Left kidney apparently normal *B*, 45 minute film Apparently good emptying of both kidneys

sumed since Subsequent excretory urograms, the latest made a year after the patient's admission, show good function bilaterally, no hydronephrosis, and good emptying The right kidney shows some distortion, the left is apparently normal (fig 6)

On discharge from the hospital the blood urea nitrogen was 13, and other parameters were also normal The urine was negative except for an occasional white blood cell in the centrifuged sediment The hematocrit had risen, without transfusion, from 35 to 43 Phenolsulfonphthalein excretion was 41 per cent in

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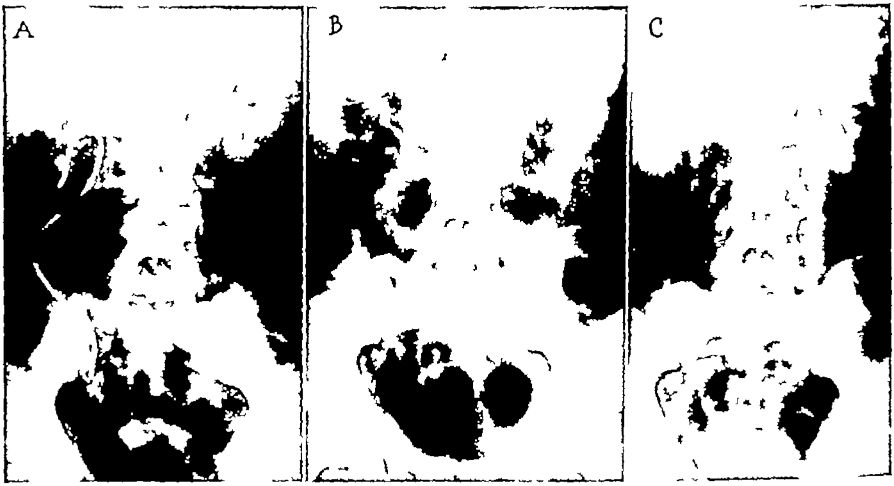

FIG 5 Excretory urograms *A*, 15 days after right nephrostomy, followed by antibiotic therapy Left kidney, which has not been operated upon, appears almost normal (Compare with figure 1, *A*) *B*, 10 days after that shown in *A*, after antibiotic therapy had been discontinued Left kidney again appears hydronephrotic *C*, 11 days after figure 5, *B* (Patient had been taking furadantin during interval) Left hydronephrosis has again regressed Right kidney shows fairly good function and seems to be draining reasonably well

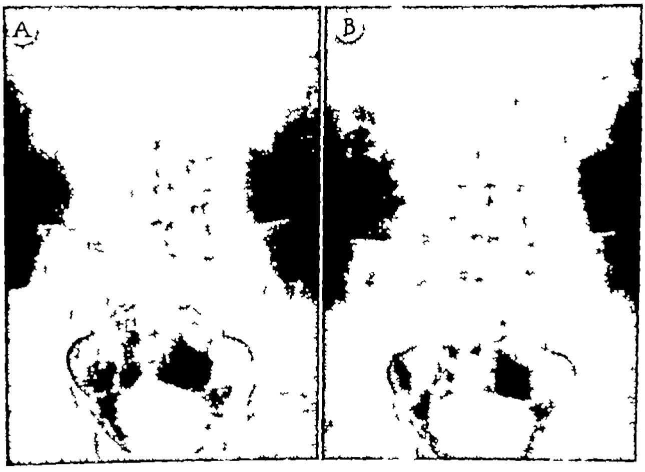

FIG 6 Excretory urograms *A*, taken little more than year after admission to hospital Right kidney shows some distortion and caliectasis, but function seems good and no gross hydronephrosis Left kidney apparently normal *B*, 45 minute film Apparently good emptying of both kidneys

sumed since Subsequent excretory urograms, the latest made a year after the patient's admission, show good function bilaterally, no hydronephrosis, and good emptying The right kidney shows some distortion, the left is apparently normal (fig 6)

On discharge from the hospital the blood urea nitrogen was 13, and other parameters were also normal The urine was negative except for an occasional white blood cell in the centrifuged sediment The hematocrit had risen, without transfusion, from 35 to 43 Phenolsulfonphthalein excretion was 41 per cent in ing as high as the kidneys Autopsies were done on two of the three patients who died and the reports follow

1) "The retroperitoneal tissues surrounding the aorta and extending from the kidneys to below the sacral promontory show almost complete replacement with a dense, raised, white fibrous connective tissue mass This tissue is 2 cm in thickness at its thickest point, and extends out to and including the ureters The ureters, aorta, and vena cava are all covered by this dense mass of fibrous tissue which is sufficient to nearly occlude the lumina of the ureters "[3]

2) "A tough fibrous plaque 1 to 2 cm thick, covering the area Its upper limit partially encircled the aorta as it passed between the crura of the diaphragm Here the fibrous tissue indented the aorta Followed downwards, the fibrous tissue spread out to the left, reaching the renal pelvis, and then passed downward, surrounding the ureter and disappearing over the pelvic brim, almost to the top of the seminal vesicles On the right it barely touched the vena cava until it reached the bifurcation of the aorta, where it spread to the right along the iliac vessels for a short distance The edges of this plaque were nowhere very definite and it seemed to peter out over a distance of about ½" The tissue had nowhere completely occluded the ureter, but had surrounded it for most of its length The other interesting result of the fibrosis was the finding that it had obstructed the lower end of the common bile duct and had caused great dilatation of the intrahepatic bile duct, being, in fact, the cause of his jaundice "[7]

The microscopic findings varied little and were, in all cases, consistent with a chronic inflammatory process In one, small abscesses were found [6] Awareness that this process may lie behind progressive renal failure, and the exclusion of more common causes of ureteral obstruction, should lead to at least a tentative diagnosis

Treatment

All of the patients reported were operated upon for relief of obstruction, but because of the varying problems they presented when they came to treatment, it is difficult to generalize about the efficacy of specific procedures The following were undertaken in this series 1) nephrectomy, 2) nephrostomy only, 3) retroperitoneal ureterolysis, with or without temporary nephrostomy, 4) ureterolysis with intraperitoneal ureteral transplantation, 5) exploratory laparotomy and biopsy only

Nephrectomy was performed on three patients Each subsequently underwent operation on the other side One had previously had bilateral nephrostomies, the nephrectomy was done a year later and retroperitoneal lysis of the ureter on the other side two years after that No late followup report is available Another also had ureterolysis, and seven years later was reported as having a normal intravenous pyelogram and negative urine, with apparently complete clinical recovery [8] The third patient had a right nephrectomy in 1944, was carried success-in the series, but all were negative They included serum agglutination tests fc typhoid, paratyphoid, Salmonella, Brucella, tularemia, typhus, Proteus 1- and Brucella abortus,[2] [6] muscle biopsies in search of polyarteritis nodosa tuberculin and coccidioidin tests,[2] and many acid-fast urine cultures

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Thirteen admission urinalyses are reported, one showed no cells, five an occasional, and three many white blood cells, the remaining four varying number of red blood cells, with an occasional white blood cell Urine cultures taken prior to instrumentation were reported in 8 cases, four were sterile and one grew Staphylococcus albus The remaining three showed mixed infections of Staphylococcus, Streptococcus hemolyticus, B aerogenes, P aeruginosa and E coli

Evidence is thus lacking on which to incriminate any previous or associated intraperitoneal, genitourinary, or systemic process as an etiologic factor

Diagnosis

The diagnosis has usually been established through investigation of a secondary effect, renal failure due to ureteral obstruction, symptoms appear only after significant uropathy has developed The absence or paucity of specific physical findings on admission has been a striking feature in all cases Admission temperatures were normal or only slightly elevated in all but one patient whose fever might have been due to a known urinary tract infection Admission blood pressures were reported for 8 patients, in four of whom the systolic pressure was 160 or higher, and in five the diastolic between 100 and 110 Presumably, the nine whose blood pressures were not recorded were not hypertensive The highest reading was 190/110 in a 40-year old man, the lowest 132/92 in a 49-year old man Although pain was a symptom in 16 of the 17 cases, tenderness could be elicited in only seven, usually of a moderate sort localized in the costovertebral angle, the flank, or the lower abdomen A palpable mass was felt in only one[6]

The laboratory data were consistent with chronic inflammation and progressive renal failure The admission white blood cell counts, noted in 10 patients, ranged from 5,800 to 16,000, only twice did the count exceed 10,000 Blood urea nitrogen or nonprotein nitrogen was elevated in 12 of the 14 cases for which they were recorded Because of the azotemia, only five had excretory urograms, all of which showed failure of excretion on one side, and one hydronephrosis on the other as well The diagnosis of extrinsic compression of the ureter was regularly established by urologic investigation Ureteral catheterization and retrograde pyelography were done on 15 patients, seven showed bilateral hydronephrosis and partial hydroureter, in seven more the condition was unilateral One patient had negative pyelography In two instances passage of the catheters was obstructed, in one there was temporary resistance which was overcome

The ultimate diagnosis has depended upon gross examination of the retroperitoneal tissue at operation, and subsequent histologic study There is a dense grayish-white sheath of fibrous tissue several centimeters thick in the retroperitoneum, impinging upon iliac vessels, aorta, vena cava, and ureters, and extend-

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The clinical course is insidious in onset and evolution, and the patient usually presents himself with symptoms of renal insufficiency due to ureteral obstruction The immediate treatment requires relief of the obstruction Permanent relief may be established by one of a number of surgical procedures or may follow treatment by *antibiotics*

The authors are deeply indebted to the authors of previous papers who took the time and trouble to provide them with up-to-date followup reports on their patients

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fully on antibiotics between 1948 and 1955, and then died of renal failure aft an attempted emergency nephrostomy, 11½ years after the first operation[7] I is apparent that every possible effort should be made to salvage renal tissu since the process is usually bilateral

Bilateral nephrostomies without other surgery were performed in the fir reported case, with death from renal failure 4 years later, after repeated ureter dilatations and antibiotic therapy[3] Another patient had an emergency unilater nephrostomy and died, also of renal failure, shortly after operation[7] Nephro tomy may be a life-saving procedure, but it cannot be expected to redeem a situation in which the renal failure has been irreversibly established at or near the point of complete insufficiency Its great contribution is to tide the patient over a critical period while definitive therapy is being instituted for permanent relief of obstruction In the case here reported it was used to divert the urine temporarily during a postoperative complication (extravasation)

Bilateral retroperitoneal ureterolysis, with or without temporary nephrostomy, was done in five patients and all did well Two have been followed for 4 years[4, 5] Ureterolysis with intraperitoneal ureteral transplantation has served excellently in three cases In two it was followed by irradiation, and in one by antibiotic therapy One has been followed for 11 years, one for seven, and one for three Another patient was simply explored and a biopsy taken, following which antibiotics were given Followup after five years indicated a good result[6]

It is apparent that lysis, by one method or another, is a useful procedure It would also appear, however, that treatment with antibiotics may be effective without surgical intervention The patient here presented will provide an excellent opportunity, as time passes, to compare the two methods It is of particular interest to note that the unoperated side showed improvement during treatment, regressed when treatment was interrupted prematurely, then improved again when it was resumed and has maintained that improvement for a year Theoretically, of course, there is no reason why a process of inflammatory origin might not be completely cured by appropriate medical therapy, if this be instituted before irreversible damage is done Unfortunately, the diagnosis cannot yet be absolutely established without operative exposure For this reason, and because some patients may require operation for drainage, it would be premature to advise categorically against surgical intervention Until more reports are available, each case will have to be judged on its merits Two principles of therapy emerge the relief of obstruction and the preservation of renal tissue If the former can be accomplished without operation, a trial on conservative treatment may be justified

SUMMARY

A clinical entity is described, increasing in incidence or more frequently recognized, in which bilateral ureteral obstruction is caused by retroperitoneal inflammation

The pathological process is of a chronic granulomatous type, going on to the development of thick fibrous tissue which envelops and compresses the ureters

The etiology is unknown

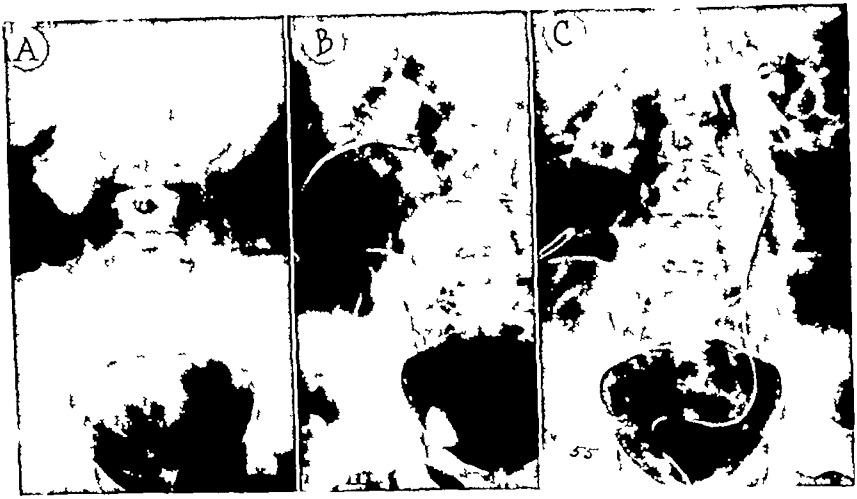

FIG 1 *A*, original pyelograms February 1952 show bilateral hydronephrosis and ureteropelvic obstruction *B*, antegrade pyelogram after right intubated ureterotomy, February 1955, ureter almost occluded *C*, antegrade and retrograde pyelogram after left intubated ureterotomy April 1955, ureter very narrow and irregular

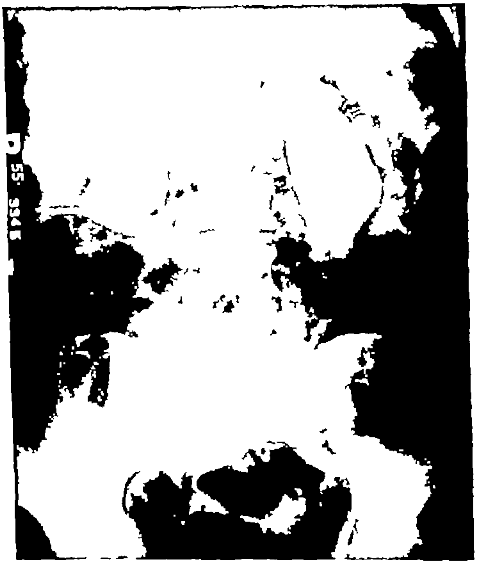

FIG 2 Antegrade pyelograms June 14, 1955 Both ureters are now completely occluded, except 3 or 4 cm at lower end

On the left side, the resting pressures ran from 6 to 12 mm Hg, and the highest pressure recorded during voiding was 20 mm Hg With the patient sitting on a commode chair, the resting pressures were much lower, the right side being about 3 mm Hg, the left often as low as zero No pressures higher than 5 mm Hg were recorded on either side, but it is hard to believe that this represents true pressure during a void The experimental conditions were not ideal, and it is possible that

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COMPLETE REPLACEMENT OF BOTH URETERS BY AN ILEAL LOOP

DAVID M DAVIS AND THOMAS F NEALON, JR

We first saw Mrs C C, aged 46, of Morgantown, Kentucky on June 5, 1955 She had suffered with chronic and recurrent bladder infections, and finally a diagnosis of bilateral hydronephrosis due to ureteropelvic strictures had been made (fig 1, *A*) On November 26, 1954 right intubated ureterotomy was performed, using a polyvinyl splint tube extending through the entire ureter The tube remained in place six weeks, but after its removal the ureter did not drain well so that the nephrostomy tube was kept in place Three months later left intubated ureterotomy was performed, again using a polyvinyl splint tube Again the ureter failed to drain, and soon no urine was entering the bladder (fig 1, *B* and *C*)

Studies in Philadelphia showed that both ureters were completely occluded except for a few centimeters at the lower end of each, and it was decided that ileal loop replacement of the ureters was the only recourse (fig 2) A short note, calling attention to the apparent ill effects of polyvinyl tubing in this case, was published at that time [1] On June 22, 1955, an ileal loop was isolated and substituted for both ureters, anastomosis being made directly with the kidney pelves On the right, the loop was carried behind the mesocolon, the cecum and ascending colon being tacked down over it after the anastomosis was completed On the left the pelvis was brought up through an incision made carefully in the mesocolon and anastomosed to the other end of the ileal loop so that the loop lay in front of the mesocolon The dependent part of the ileal loop was anastomosed to the dome of the bladder with a wide ostium Ileal continuity was reestablished by end-to-end anastomosis Both fallopian tubes were crushed, divided and ligated, since pregnancy would dangerously disturb the new arrangements Various peritoneal sutures were taken to prevent any possibility of internal herniation or strangulation A retention catheter was placed through the urethra into the bladder The presence of inflated 5 cc balloons of the Foley nephrostomy catheters aided greatly in locating and freeing the kidney pelves

On July 5, 1955 the nephrostomy tubes were clamped (figs 3 and 4) As there was some difficulty in voiding, transurethral resection of the vesical orifice was carried out on July 12, 1955 On July 20, 1955, the nephrostomy tubes were removed and there was drainage of urine for only 4 or 5 hours

Before the nephrostomy tubes were removed intrapelvic pressures were determined, using a strain gauge and oscilloscope On the right side, with the patient in bed, resting pressures were observed as about 7 to 10 mm Hg, while during voiding into a bedpan the pressure rose to 30 or 40 mm as a rule, once reaching 60 mm Hg The fall to resting pressure occurred very quickly after the void

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Read at annual meeting of American Urological Association, Pittsburgh, Pa, May 6-9, 1957

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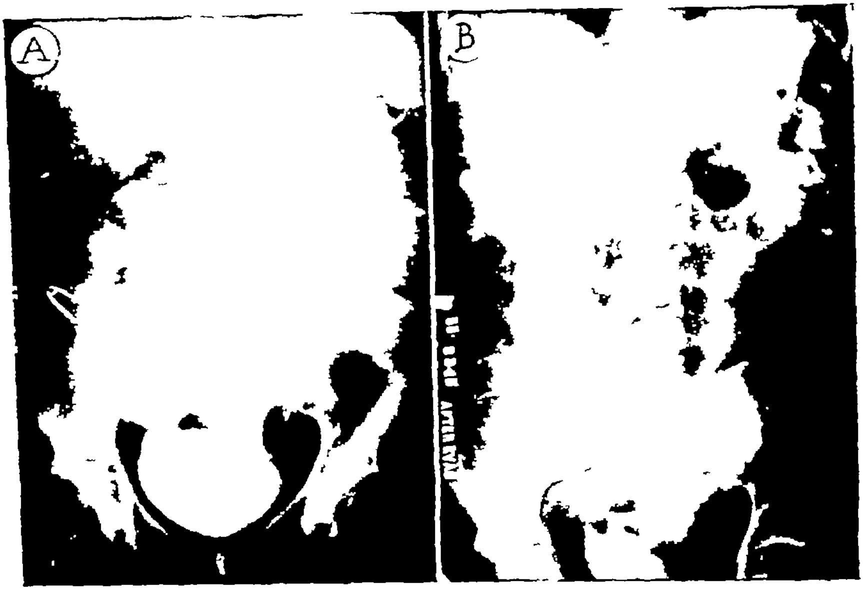

FIG 4 A cystogram made July 6 1955 Note moderate reflux up both limbs of ileal loop *B*, film taken after patient voided Some solution remains in ileal loop Compare with pressure studies made during voiding

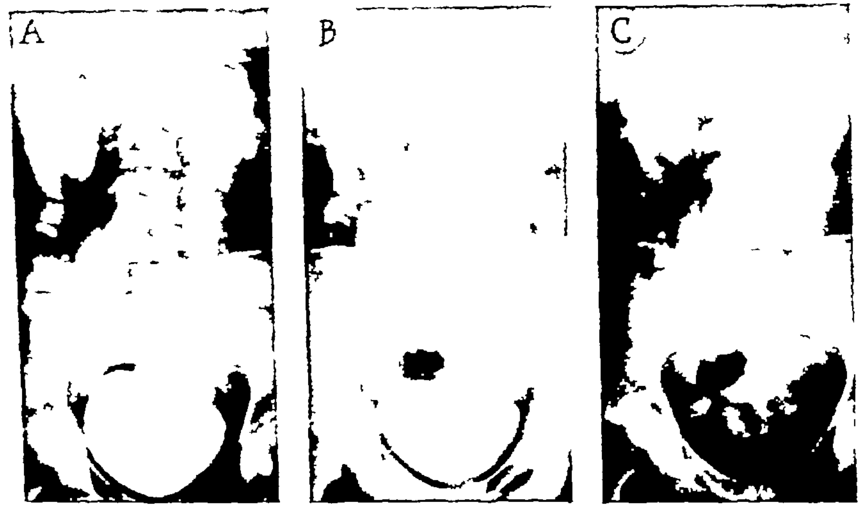

FIG 5 Cystogram made nine months after removal of nephrostomy tubes *A* 500 cc has been injected *B* 250 cc has been removed from bladder *C* film taken 15 minutes after emptying bladder and removing catheter

capacity of the ureters After the patient returned home on July 29 1955 she felt generally well but the voiding difficulty persisted and a moderate sized incisional hernia developed She returned to the Jefferson Hospital April 24 1956 A cystometric test showed a low expulsive force as is seen in large diverticula of

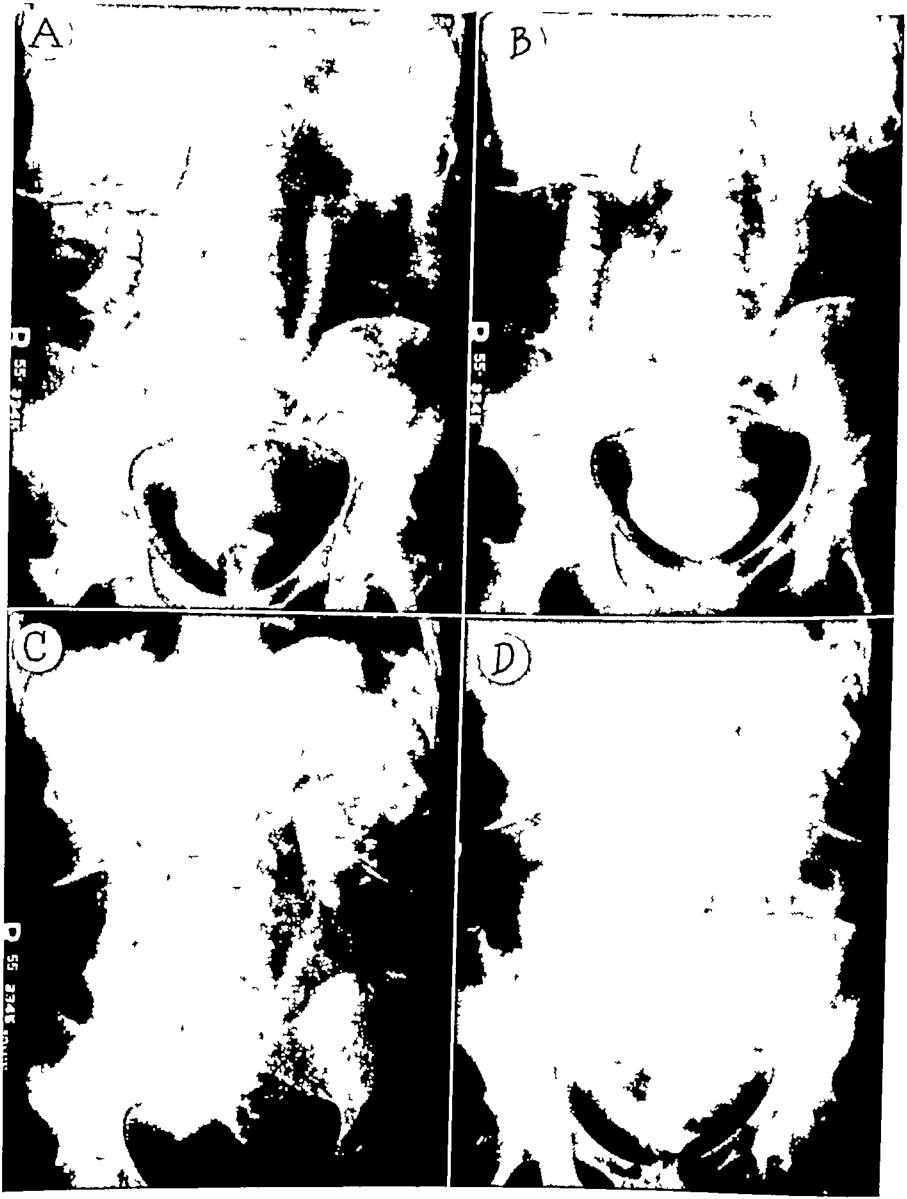

FIG 3 *A*, right antegrade pyelogram, July 5, 1955, thirteen days after operation Some reflux up left limb of ileal loop *B*, left antegrade pyelogram a few minutes later Right pelvis partially emptied, bladder filled *C*, film taken 10 minutes after *B*, both nephrostomy tubes clamped Right pelvis almost empty Left pelvis much smaller Patient has voided *D*, film taken 10 minutes after *C*, patient erect Right empty, left pelvis still smaller

some leakage in the connections developed while getting the patient out of bed However there does seem to be a consistent difference between the peristaltic and the antiperistaltic side, in favor of the former

Voiding occurred usually in two or three stages, due no doubt to the large

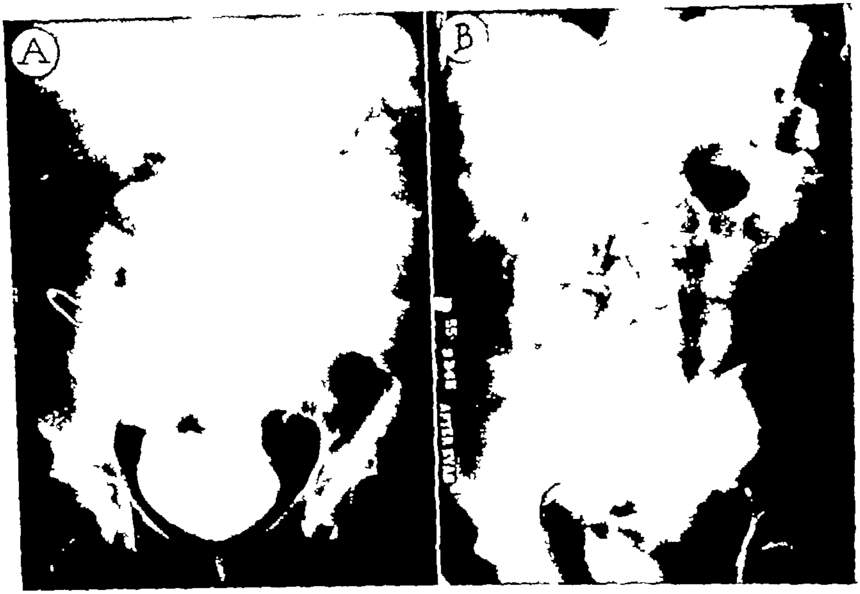

FIG 4 A, cystogram made July 6, 1955 Note moderate reflux up b[illegible] B, film taken after patient voided Some solution remains in ileal loop [illegible] pressure studies made during voiding

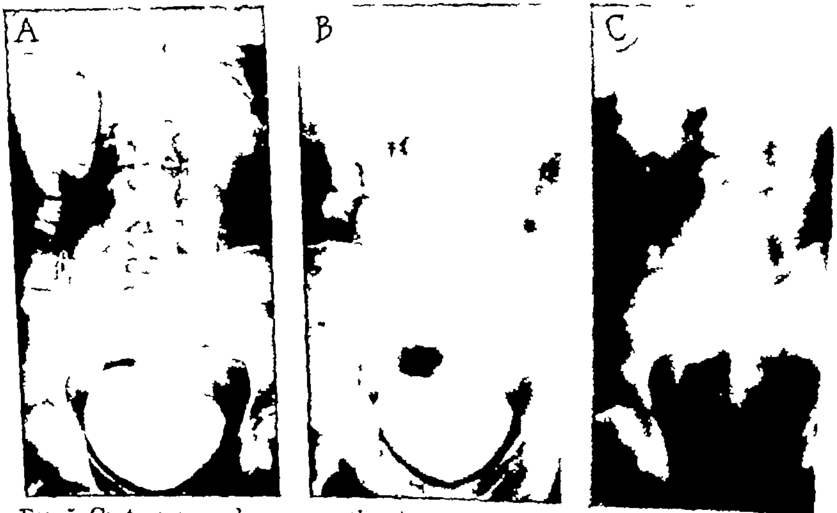

FIG 5 Cystogram made nine month after [illegible] been injected B, 250 cc has been removed fro[illegible] emptying bladder and removing catheter

capacity of the ureters After the patient returned [illegible] felt generally well but the voiding difficult[illegible] sional hernia developed She returned to the Jefferson Hospital [illegible] cystometric test showed a low expulsive force [illegible]

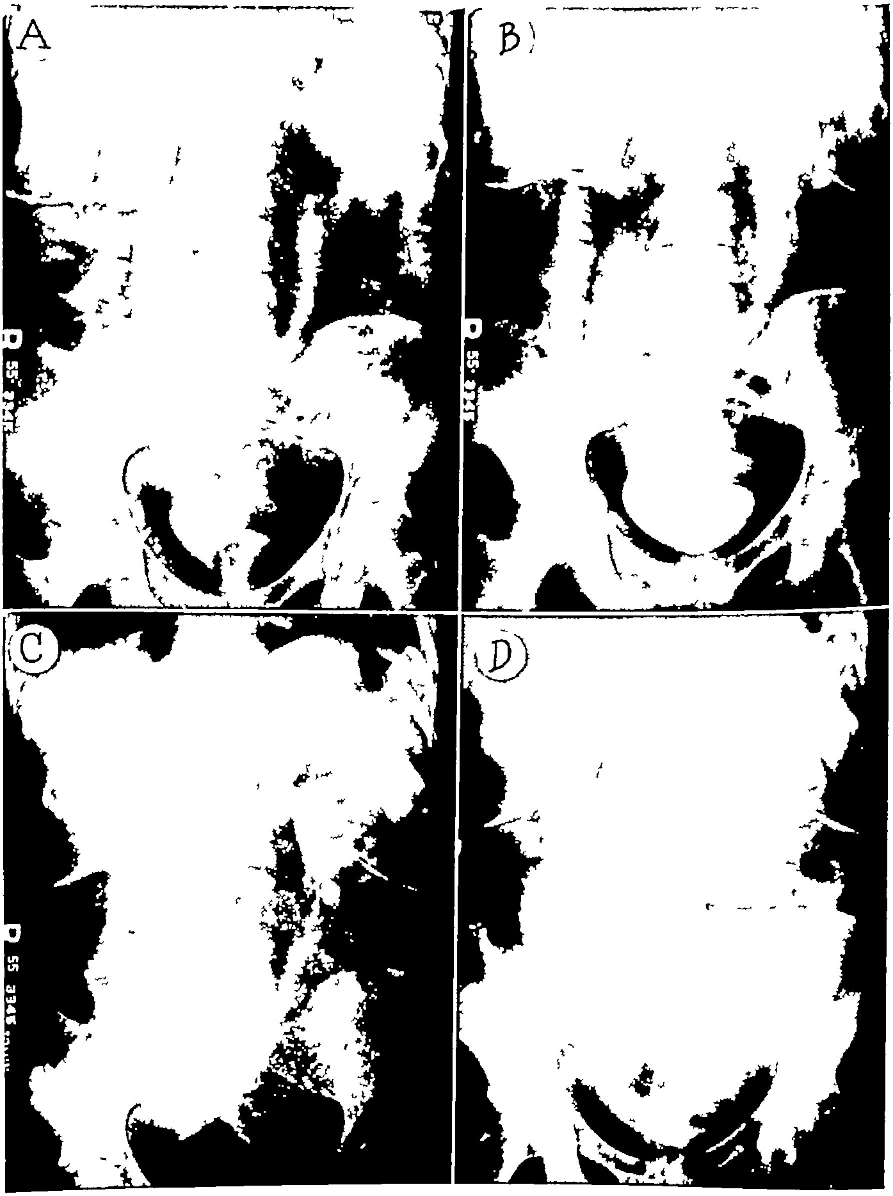

FIG. 3. *A*, right antegrade pyelogram, July 5, 1955, thirteen days after operation. Some reflux up left limb of ileal loop. *B*, left antegrade pyelogram a few minutes later. Right pelvis partially emptied, bladder filled. *C*, film taken 10 minutes after *B*, both nephrostomy tubes clamped. Right pelvis almost empty. Left pelvis much smaller. Patient has voided. *D*, film taken 10 minutes after *C*, patient erect. Right empty, left pelvis still smaller.

some leakage in the connections developed while getting the patient out of bed. However there does seem to be a consistent difference between the peristaltic and the antiperistaltic side, in favor of the former.

Voiding occurred usually in two or three stages, due no doubt to the large sure readings in this case suggests that the peristaltic action of the ileal loop protected the left kidney and kept the intrapelvic pressure down, although the roentgenologic evidence gives no appreciable indication of such a difference between the two sides 5) Even the high pressure existing in the right kidney pelvis during voiding did not prevent the rapid closing of the nephrostomy sinus after the tube was removed

We recommend that studies as thorough as possible be carried out on every case of ileal loop substitution for the ureter, especially those in which a nephrostomy exists, so that we may learn more about this fascinating subject

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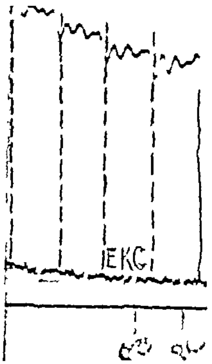

FIG 6 Pressure curve in right nephrostomy tube Lower tracing is an electrocardiogram Upper tracing shows respiratory and pulse waves, and other waves 3 or 4 to each heart beat

the bladder On April 27, 1956 the incisional hernia was repaired, and on May 1, 1956 the transurethral resection was repeated and an internal urethrotomy to size 41F carried out, to reduce urethral resistance as much as possible At this time the ostium between the ileal loop and the bladder was observed cystoscopically and seen to be in good condition Convalescence was uneventful and the patient left the hospital May 10 1956

Since then she has improved slowly but steadily The temperature, blood urea nitrogen, carbon dioxide combining power and blood chlorides have been normal at all times The urine has never become sterile, but very little medication is now required The urethra has been dilated a number of times and the latest report is that "The urine flushes out better than it has any time before and I have never had any more pain in the bladder " She has followed her usual occupation as a school teacher during the entire season of 1956–57

Roentgenograms showed that no opaque material whatever entered either ureter from the pelves before operation After operation urine flowed freely from both kidneys into the bladder and no difference between the two sides could be observed, although the flow from the right kidney was counter to the previous direction of peristalsis in the ileal loop Cystography, 9 months after operation, showed prompt reflux into both kidney pelves Evacuation films showed that urine left the pelves steadily, but that emptying took a long time (fig 5) Obviously a good deal of urine remained in the pelves and the ileal loop

The pressure curves show respiratory and pulse waves as would be expected, but in addition there are other waves of small amplitude occurring at the rate of 3 or 4 to each heart beat (fig 6) We cannot say whether these represent contractions of the pelvic musculature, or are simply artefacts

This case appears to support a number of interesting points 1) Apparently some people are allergic to polyvinyl, and in these cases a fibrous reaction may obliterate the ureter completely 2) An ileal loop may be anastomosed directly to the renal pelvis, and substitute for the entire ureter in at least a fairly satisfactory manner 3) The renal parenchyma resists high intrapelvic pressures very well if these high pressures occur only at intervals, with normal pressures the rest of the time 4) The evidence obtained from the pres-

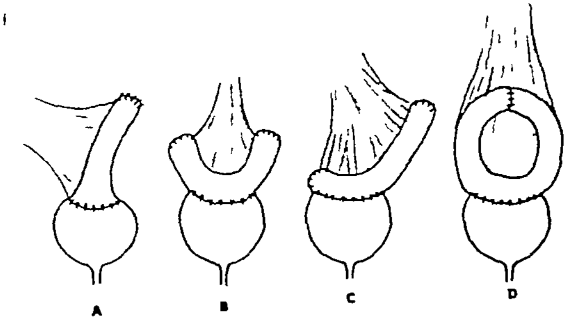

FIG 1 Methods of closed loop ileocystoplasty *A*, cat-tail type *B* T type *C*, off-center isoperistaltic anastomosis *D*, ring type

segment of ileum was anastomosed to the bladder as an open sheet, in the majority a closed tube was anastomosed to the bladder in varying positions (fig 1) Hanley[10] has noted that urine is retained in the closed types of reconstruction It would appear that an open patch of ileum would empty itself more efficiently However, the reconstructed bladder must not only be able to empty, but must also be able to contain urine in a physiologic manner, at low intravesical pressures and with minimum reabsorption of electrolytes

The purpose of this investigation was to evaluate these physiologic responses

EXPERIMENTAL STUDIES

Method of procedure Eight dogs, ranging in weight from 10 to 19 kg , were used for these experiments Five were males and three were females In each dog the bladder was mobilized and then subtotally resected leaving a small stump The level of excision was just above the trigone, so that the ureteral orifices were undisturbed A 12 cm segment of ileum, approximately 30 cm from the ileocecal valve, was isolated with an intact pedicle of mesentery The continuity of the bowel was restored by end-to-end anastomosis The isolated ileum was then incised on its antimesenteric border The free border of the intestinal patch was sutured to the vesical stump by a mucosa-to-mucosa technique, forming a bladder composed principally of ileum (fig 2) In the immediate postoperative period urinary drainage was maintained in the female dogs by urethral catheter In the males, a stab wound was made in the dome of the new organ and a cystotomy tube inserted The peritoneal cavity was closed without drainage All tubes were removed on the seventh or eighth postoperative day In all instances the animals voided without apparent difficulty, were continent and behaved normally Intravenous urography was done on all animals Normal renal morphology and function was noted in all instances (fig 3, *A*) The retrograde cystogram demonstrated in figure 3, *B* is typical of the appearance of the bladder after ileocystoplasty After a period of convalescence that varied from three weeks to nine months, the altered bladder of each animal was studied by cystometry, for electrolyte absorption and for histologic changes in the transplanted intestine

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FUNCTIONAL ANALYSIS OF THE BLADDER AFTER ILEOCYSTOPLASTY I

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The use of an isolated intestinal segment to augment bladder capacity, or ileocystoplasty, merits serious consideration Contracture of the bladder with decreased capacity, regardless of etiology, usually produces severe urinary symptoms and bilateral renal destruction The important etiologic factors are interstitial cystitis, tuberculous infection, chemical or radiation damage, and persistent hypertonic neurogenic dysfunction Extensive subtotal resection of the bladder may also result in limited fluid capacity The renal damage seen with contracture of the bladder is a consequence of two mechanisms 1) recurrent and chronic pyelonephritis, induced by reflux of infected vesical urine, and 2) hydronephrosis resulting from persistent high intravesical pressure acting as an obstruction to flow of urine

Until recently the prevalent treatment for the disease complex caused by contracted bladder was diversion of the urine, either to the large bowel or skin, or the use of an indwelling urethral catheter, eliminating the bladder as a reservoir Among the undesirable aspects of diversion of urine from the bladder are 1) renal infection by organisms from the skin or feces, 2) stricture of anastomotic sites, and 3) electrolyte imbalance following ureteral transplants to bowel

Ileocystoplasty may be a possible solution to these difficulties The experimental use of this procedure was first reported by Tizzoni and Foggi[1] in 1888, but the clinical results in that period were poor However, recent clinical and experimental applications as reported by Couvelaire[2] and Cibert[3] in France, Tasker,[4] Pyrah,[5] and Wells[6] in England, Freitas and Sadi[7] in Brazil, and Ferris[8] and Shoemaker and Marucci[9] in the United States are promising These investigators used different techniques for ileocystoplasty In some instances the isolated

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mined (fig 4) The normal dog bladder was found to respond to increased intravesical fluid in a manner similar to the human bladder The detrusor muscle relaxed to accommodate fluid at low pressure, then as capacity was reached the intravesical pressure increased sharply Analysis of observations shows that the average bladder capacity in normal dogs was 124 cc

Cystometrograms were then done in six dogs in the postoperative period after ileocystoplasty without drugs and then after administration of urecholine and

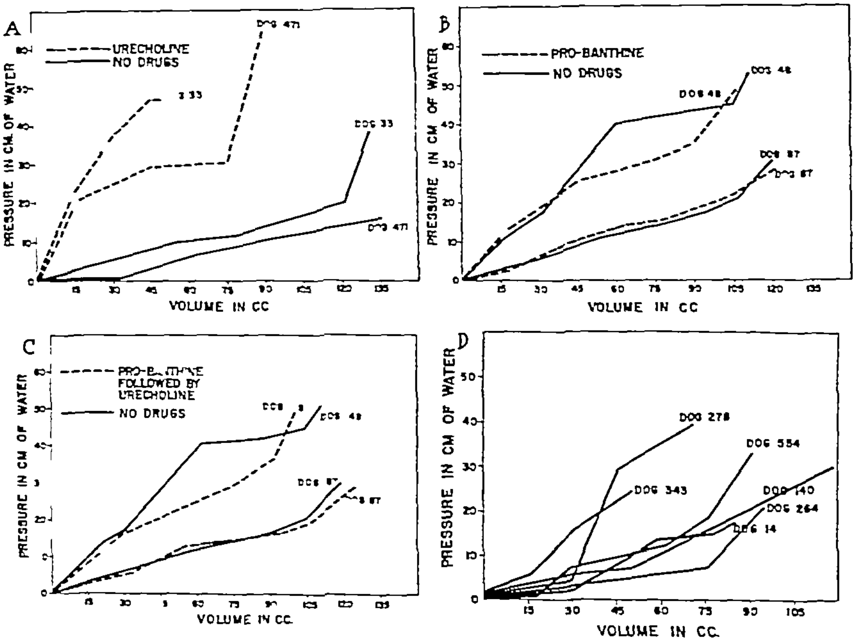

FIG 4 Cystometrograms of normal dogs A, before and after administration of urecholine B before and after administration of urecholine C before and after administration of pro banthine followed by urecholine Note blockage of usual urecholine effect by pro-banthine D, after ileocystoplasty

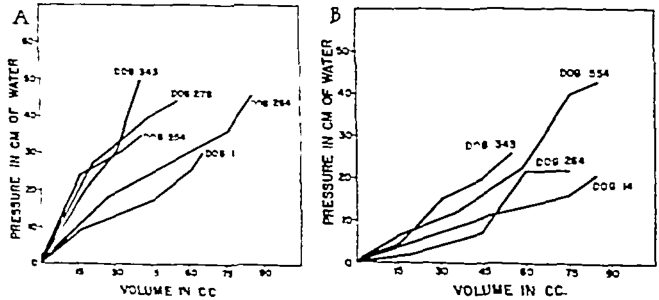

FIG 5 Cystometrograms obtained after ileocystoplasty in dogs 1, administration of urecholine Note increased pressures and diminished capacities B, following administration of pro banthine after ileocystoplasty Curves approximate cystometrograms obtained without drugs

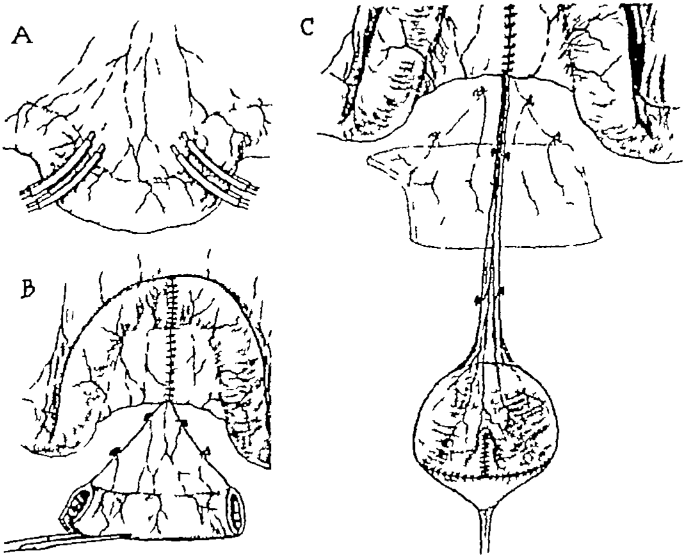

FIG 2 Open sheet method of ileocystoplasty *A*, isolated ileal segment Incision on anti mesenteric border *B* and *C*, completed anastomosis Ileum that is surplus for anastomosis to bladder stump is sutured to itself in midline of anterior plane

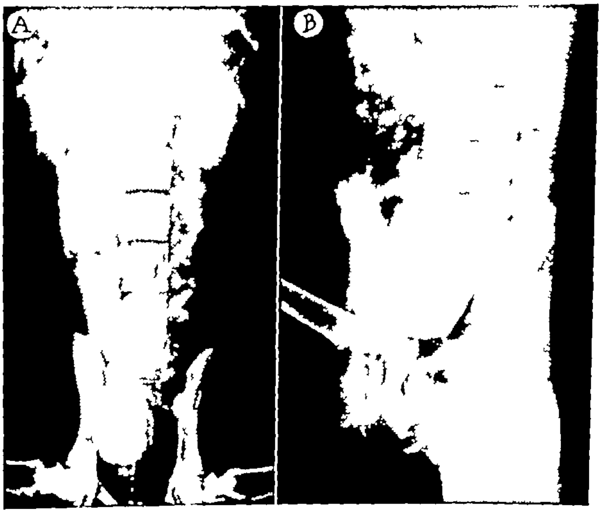

FIG 3 Dog No 264 *A*, intravenous urogram three and a half months after ileocysto plasty *B*, retrograde cystogram, oblique view

1) Cystometric studies In order to obtain standard controls, cystometrograms were done in five normal dogs ranging in weight from 15 to 17 kg The response of the normal dog bladder to a cholinergic drug (bethanechol chloride, urecholine) and an anticholinergic drug (propantheline bromide, pro-banthine) was also evaluated Intravesical pressures were measured by a water manometer All measurements were read directly from the manometer tube Normal standards were obtained and effective dosages of urecholine and pro-banthine were deter-

TABLE 1 *Average values of electrolyte and urea nitrogen in normal dogs and those after ileocystoplasty*

	Range Of Reported Normal Values meq/L	Average Values Of Normal Control Dogs meq/L	Average Values After Ileocystoplasty meq/L
Sodium	135–160	151	153
Potassium	3 7–5 8	4 5	4 4
Chlorides	99–110	114	117
CO content	18 7–22 0	19 7	17 2
Blood urea nitrogen	10–20 mg %	19 mg %	22 mg %

TABLE 2 *Details of electrolyte studies in normal and post ileocystoplasty dogs*

Dog	CO$_2$ Content mm/L	Sodium meq/L	Potassium meq/L	Chlorides meq/L	B U N mg %
No 264 Ileocyst	18 7	157	4 4	114	16
No 554 Ileocyst	15 2	150	4 0	119	24
No 343 Ileocyst	15 4	156	4 2	122	27
No 14 Ileocyst	17 3	148	4 4	114	20
No 26 Ileocyst	19 5	154	4 9	117	23
No 1 Normal control	21 2	156	4 6	111	21
No 2 Normal control	18 4	148	4 0	117	20
No 3 Normal control	19 6	149	5 0	115	16

ileocystoplasty (tables 1 and 2) show that the postoperative electrolyte plasma values are generally normal with only a few slight abnormalities This is in accord with the excellent clinical condition of the animal after operation

These results, however, do not preclude the possibility that absorption from the bladder did take place but was not significantly reflected in the plasma values To determine the extent of absorption from the bladder in our dogs, studies were undertaken using radioactive sodium (Na^{24}) These experiments are detailed in a separate report, but in summary it can be concluded that the absorption that takes place does not alter sodium balance[12]

3) Anatomic changes in transplanted intestine after ileocystoplasty The gross appearance of the bladder after ileocystoplasty resembles a normal bladder (fig 6) After several weeks postoperatively it is difficult to differentiate between the intestinal segment and the bladder stump This lack of differentiation is apparent on both the serosal and mucosal surfaces

In the five animals sacrificed for study, microscopic structure of the kidneys was normal in all the animals (fig 7)

Progressive anatomic changes take place in the ileal sheet as demonstrated by histologic sections taken from five dogs at different stages in the postoperative period Flattening of the epithelium with absence of intestinal villi is seen (fig 8, A) Specific staining demonstrates marked atrophy of the mucus glands with diminished mucus production Grossly there is a marked diminution of

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[1] Sinatra T J and Weinberg S R Functional analysis of the bladder after ileocystoplasty II To be published

pro-banthine Although true residual urines are impossible to obtain in dogs, on random catheterization of the dogs after ileocystoplasty only small amounts of urine were obtained ranging from 5 cc to 20 cc Examination of the graphs obtained reveals that the altered bladder can respond to changes in volume by an increase in intravesical pressure in a manner analagous to the bladders of normal dogs (fig 4, *D*) The average fluid capacity of the reconstructed bladder was 86 cc as compared with 124 cc in our normal dogs It may well be that the bladder capacity is augmented with passage of time in the postoperative period The animals with the longest postoperative interval (No 140) had the largest bladder capacity, 120 cc, whereas dogs Nos 343 and 278, which were earliest in the postoperative period, had the smallest bladder capacities of 50 cc and 70 cc respectively

Cystometry 10 minutes after the administration of a subcutaneous injection of 2 5 mg of urecholine disclosed a definite increase in intravesical fluid pressure with a decrease in bladder capacity in all instances (fig 5, *A*) The potency of the drug was affirmed by greatly increased salivation Since almost all of the dog bladder after ileocystoplasty consists of intestine, it appears that the displaced intestinal sheet retains an ability to respond to cholinergic influences by sustained contraction in a manner analagous to the detrusor muscle of normal dogs

In a similar series of experiments, 15 mg pro-banthine, an anticholinergic drug, was injected intramuscularly It already has been shown that 15 mg of pro-banthine was an effective dose When it is administered prior to the injection of urecholine, it effectively eliminates excess salivation and the increase in bladder pressure and the decrease in bladder capacity caused by urecholine (fig 4, *C*) After 20 minutes its effect on the bladder altered by ileocystoplasty was also studied by cystometry Results indicate, as in the normal dogs, there is essentially no change in the cystometrogram after the injection of pro-banthine, bladder capacity was not increased (fig 5, *B*) Therefore, while pro-banthine may block contractions due to cholinergic influences, it apparently does not increase bladder capacity after ileocystoplasty

2) Absorption of electrolytes from the bladder after ileocystoplasty In order to determine any deleterious absorption of electrolytes from the intestinal mucosa of the reconstructed bladder, electrolyte studies were undertaken in the postoperative period These studies included A) determination of the plasma concentrations of urea, potassium, sodium chlorides, and carbon dioxide content, B) study of *radioactive sodium* (Na^{24}) *absorption after its instillation into the* reconstructed bladder

Normal plasma electrolyte values in dogs are not exactly identical to those in human plasma In our laboratory the concentration of sodium and chloride in dog plasma is greater than that found in the human, a finding in accord with observations by others[11] Also, dog blood has a slightly lower pH

The normal dog values compared with those obtained from the dogs after

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[11] Spector, W S Editor of Handbook of Biological Data Prepared under the direction of the Committee on the Handbook of Biological Data, Division of Biology and Agriculture, the National Academy of Sciences, the National Research Council Philadelphia W B Saunders Co , 1956

A 48-year-old white woman (Long Island College Hospital No 27487) had urinary frequency, dysuria and severe suprapubic pain with increasing difficulty for 15 years culminating in constant urinary dribbling (fig 9, *A*) Severe contracture of the bladder, bilateral hydroureters and caliectasis were present Ileocystoplasty was accomplished March 9, 1956 using the open patch technique Because of its small size the bladder was merely incised transversely at the dome, and a wedge removed for biopsy The ileal patch was then sutured end-to-end to the lips of the bladder incision The vascular pedicle of the ileal patch was brought through the posterior peritoneum and the peritoneum closed without drainage The reconstructed bladder was placed completely in the extraperitoneal space Urinary drainage was maintained by a large indwelling Malecot urethral catheter A Penrose drain was placed in the suprapubic space

The patient tolerated the operation without incident The urethral catheter was removed on the seventh postoperative day, the Penrose drain the next day when it was apparent that the patient was able to void without difficulty and that there was no suprapubic urinary drainage Although minimal urinary frequency remains, there has been definite amelioration of symptoms since the operation (fig 9, *B*) Almost a year later the plasma, urea and electrolyte values were normal, and (fig 9, *C*) an excretory urogram demonstrates prompt visualization of both kidneys in five minutes and regression of ureteral and calyceal dilatation

The other patient had a similar history A 49-year-old white woman had been treated at Kings County Hospital (No 13391-57) for severe urinary frequency and dysuria of 11 years' duration A Hunner's ulcer had been seen during a cystoscopic examination four years before surgery An extraperitoneal rupture

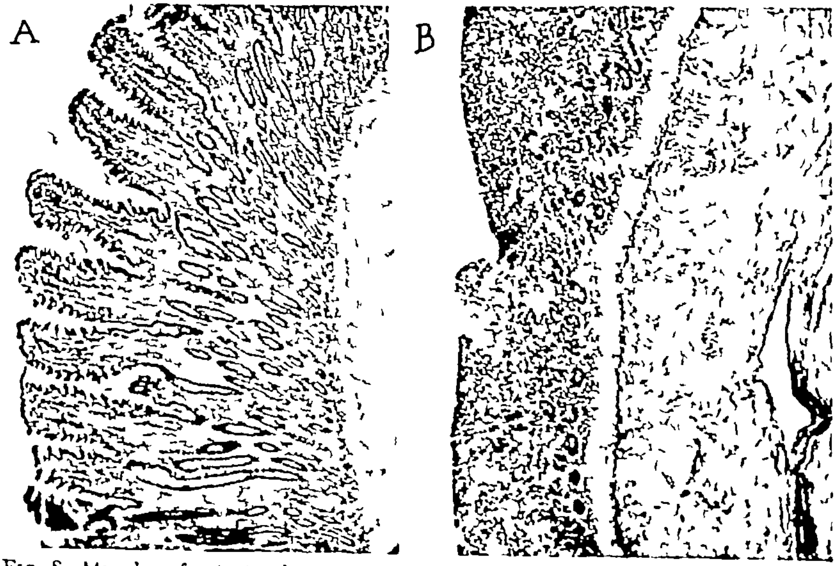

FIG 8 Atrophy of intestinal mucosa after ileocystoplasty A normal mucosa of dog ileum *B* section of ileal sheet nine months after ileocystoplasty Note absence of villi and atrophy of mucus glands of mucosa

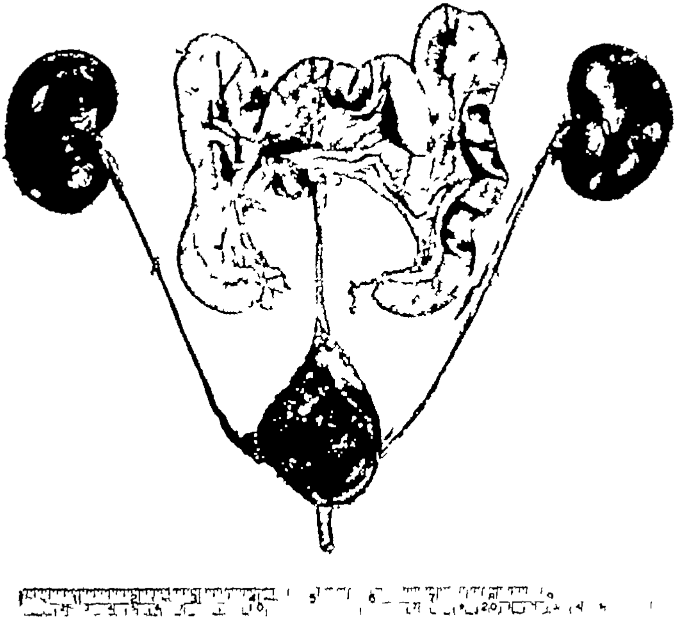

FIG 6 Autopsy specimen, nine months after ileocystoplasty, demonstrates normal appearance of kidneys and piriform shape of altered bladder

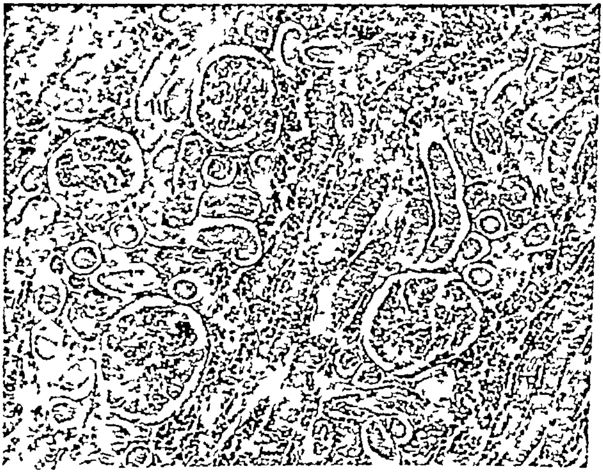

FIG 7 Section of dog kidney seven months after ileocystoplasty

mucus noted in the urine in the postoperative period This decrease in mucus formation has also been reported by Sadi[13]

CASE REPORTS

The case histories of two patients will be presented briefly, to illustrate the clinical value of ileocystoplasty pain and had good control of urine Urinary frequency is still present but it is hoped that improvement will be progressive An excretory urogram taken six weeks after the operation demonstrates normal renal function and morphology The piriform shape of the post-ileocystoplasty bladder may be due to the fact that resection of the upper third of the damaged bladder allowed an adequate stoma for anastomoses and perhaps prevented the formation of an ileal diverticulum (fig 10, *B*)

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[13] Sadi, A O emprego de segmento intestinal excluido como substituto bexiga e sua utilizacao na aumento da cavidade vesical Escola Paulista de Medicina, Sao Paolo, 1955, p 161

CONCLUSIONS

Eight dogs, subjected to ileocystoplasty using the ileal sheet technique, survived without incident and behaved as normal dogs

Cystometric studies of the bladder after ileocystoplasty showed approximately 69 4 per cent return of normal bladder capacity with satisfactory response to stretch and drugs

Absorption from the reconstructed bladder, as studied by radioactive sodium (Na^{24}), showed absorption of sodium decreasing with prolongation of the postoperative period Absorption is compensated for by renal excretion since plasma values of sodium were normal Plasma concentrations of urea and other electrolytes were also generally normal with only few slight abnormalities

The reconstructed bladder develops a piriform vesical appearance The ureters and kidneys remained normal Atrophy of the intestinal mucosa and decrease of mucus production are progressive in the postoperative period

Two patients with contracture of the bladder due to interstitial cystitis treated by ileocystoplasty had satisfactory palliation

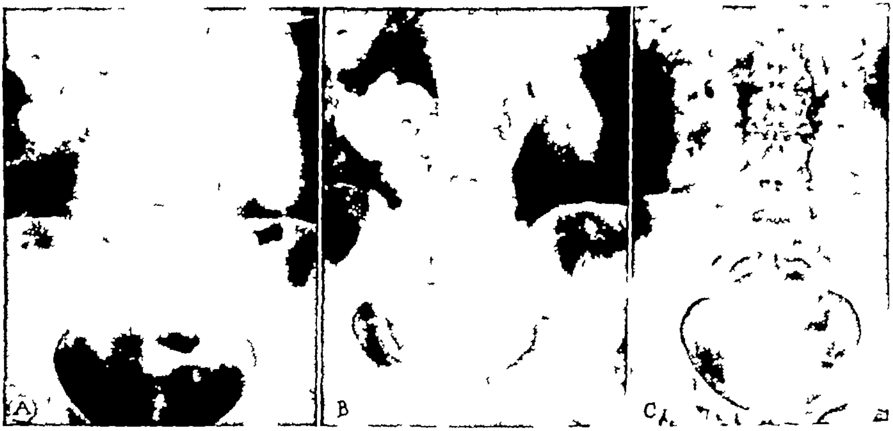

FIG 9 Case 1 *A*, preoperative excretory urogram demonstrates advanced contracture of bladder, bilateral ureterectasis, pyelectasis and caliectasis *B*, retrograde cystogram six months after operation, 150 cc contrast medium introduced by gravity technique Bilateral ureteral reflux still present *C*, excretory urogram one year after ileocystoplasty Note prompt visualization of both kidneys in five minutes and regression of previously noted ureteral and calyceal dilatation

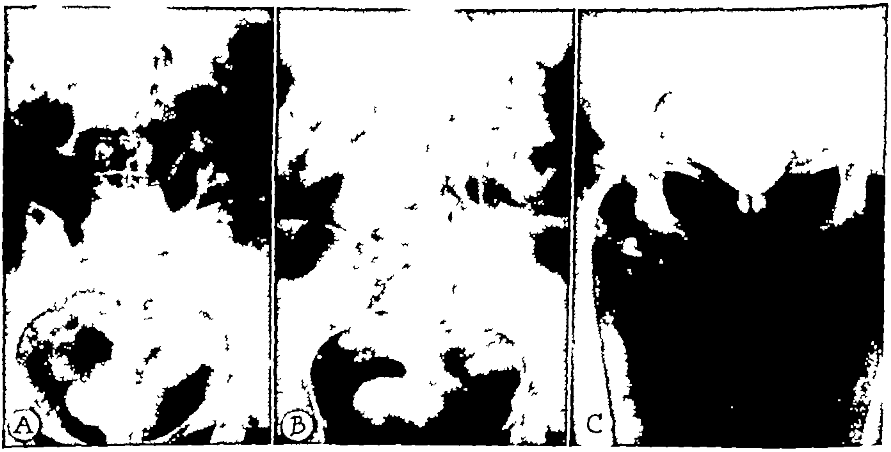

FIG 10 Case 2 *A*, excretory urogram one year before ileocystoplasty Bladder capacity 150 cc *B*, excretory urogram six weeks after ileocystoplasty Five minute film Note unaltered normal renal function and morphology *C*, one-hour excretory cystogram Note piriform shape of bladder after ileocystoplasty

of the bladder followed a therapeutic dilatation for this condition one year before the operation After this incident her bladder became so irritable that a urethral catheter could not be tolerated Constant urinary dribbling was present, as well as severe vesical and suprapubic pain Total bladder capacity after anesthesia was 150 cc (fig 10, *A*) Ileocystoplasty was done February 1, 1957 In this instance the entire dome, approximately the upper third of the bladder, was resected The resected area was pale, very firm, and composed of dense scar tissue and so removed rather than to leave detrusor muscle incapable of function The ileal patch was then sutured to the remainder of the bladder When the urethral catheter was removed after ileocystoplasty, the patient was free of suprapubic

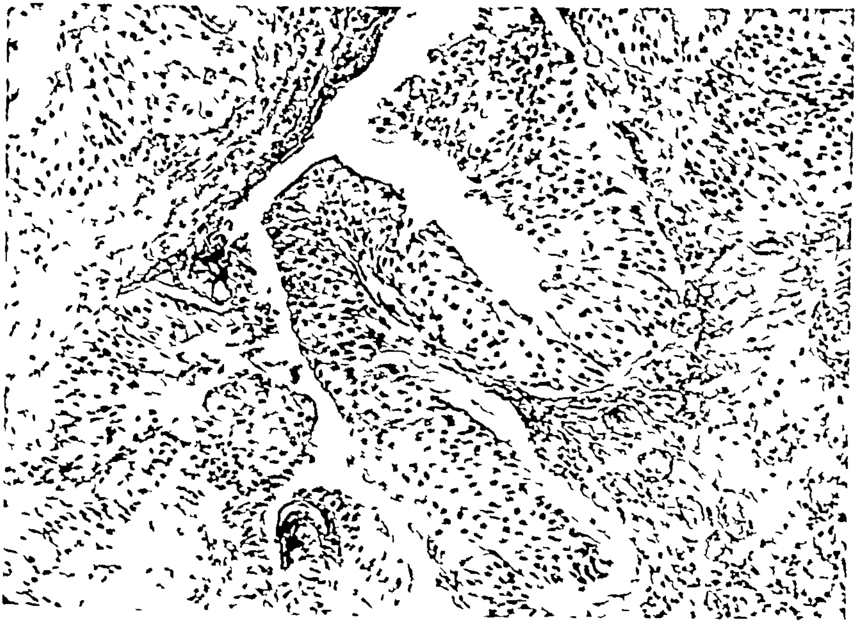

FIG 1

been removed a small papillary tumor was found on the floor of the bladder near the left ureteral orifice A second tumor was seen just inside the bladder neck on the right Bilateral pyeloureterograms were normal On August 9, 1954, under spinal anesthesia, the two tumors were removed by transurethral resection and the base of each fulgurated

Pathological report (Dr C A Hellwig) The specimen submitted consists of two pieces of soft tissue One is translucent Microscopic The bladder tumors are composed of very narrow fibrous strands which contain dilated blood vessels The epithelial cells are arranged in broad sheets The cells have a clear cytoplasm and a dark stained nucleus No mitotic figures are seen and the size of the nuclei is quite uniform In the smaller piece the surface is papillary, the cells are also quite regular in form, they cover the fibrous septa in many layers Diagnosis Papillary carcinoma of the bladder, grade 1 (fig 1)

SUMMARY

Papillary carcinoma, grade 1, in a 15 year-old girl with two separate tumors in the bladder, is reported

Treatment consisted of transurethral resection of the two tumors and fulguration of the base

The patient has had no recurrence of the tumor for nearly three years and appears quite well

Papillary carcinoma of the bladder in a teen-ager is a very rare disease

327 Chestnut St, Halstead, Kans

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BLADDER CARCINOMA IN A TEEN-AGED GIRL

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Primary papillary carcinoma of the bladder in children is a very rare disease In 1924 Deming reviewed the literature on primary bladder tumors in children and reported only one case in the first decade of life This case was described by Charon and Ledeganck The Carcinoma Registry of the American Urological Association contained two cases in 1949 The Armed Forces Institute of Pathology reported one case in 6,000 below the age of 12 in an 11-year-old child * Lowry, Soanes and Forbes reported papillary carcinoma grade 1, in a 6-year-old boy in 1955 They stated that theirs was the fifth such case in the literature

Rathbun in 1937 found a total of only 75 cases of all types of bladder tumor in children up to that time In 1950 Waller and Hamer studied 373 cases of bladder tumor and found none in children The youngest was 20 years of age and only three were below 27 years of age

The rareness of this type of tumor in the very young patient prompts us to report our case

CASE REPORT

B G , a 15-year-old girl, was admitted to the Halstead Hospital on August 5, 1954 with the complaint of repeated attacks of gross hematuria She first saw blood in the urine on June 10, 1954 This lasted for only two voidings and then ceased One month later she again had gross hematuria associated with some burning and frequency The urine again became clear after 24 hours and remained clear until August 4, 1954 at which time we first examined her and advised cystoscopy

The patient's appetite had been poor and she was constipated She had lost 10 pounds of weight during the preceding three months

The patient had had pertussis, measles, mumps and chickenpox Her tonsils had been removed at the age of 12 In October 1954 the appendix was removed Other past history and family history were not unusual

The red blood count was 3,330,000 and the white and differential counts were normal Urinalysis grossly bloody, specific gravity 1 021, albumin 4 plus, sugar negative, microscopic—loaded with red blood cells, no casts Culture of the urine was reported as no growth

The patient was well developed and well nourished Her temperature was 98 6F Pulse was 72 per minute Physical examination revealed a normal 15-year-old girl with no positive findings

On August 6, 1954 cystoscopic examination was made After blood clots had

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* Personal communication from Dr Elbert DeCoursey to Drs Lowry, Soanes and Forbes (J Urol , 73 307, 1955)

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HYPOSPADIAS: THE PRINCIPLE OF THE THIRD DEGREE

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The literature on hypospadias describes many methods of repair and the good results are emphasized. No one seems willing to give an analysis of his difficulties and his complications. The multiplicity of operations which have been recommended for the repair of hypospadias reflects the difficulties of surgical correction and the complications ensuing from various procedures. The actual technique of the repair of hypospadias deformities has become largely a matter of individual preference of the operating surgeon. Procedures successful or satisfactory in the hands of one surgeon may be less successful or less satisfactory for another. Reviews of the literature and discussions of the embryology have been adequately covered in other papers. No attempt will be made to duplicate these efforts.

Irrespective of the individual techniques which have been devised, the three basic principles of urethral reconstruction are 1) the use of a local skin flap, 2) the use of a pedicle flap formed into a tube, and 3) the use of a free graft. Let us first evaluate the various steps necessary for adequate repair of hypospadias.

All operative procedures will fail unless adequate correction of the chordee is obtained. This has been stressed by all the authors in the field and means the meticulous excision of all restraining tissue, fascia and skin from the glans to behind and proximal to the urethral meatus (fig. 1). Since this is such a necessary component of successful repair, it is to be accepted that adequate resection of the chordee is a fairly well established surgical procedure and usually does not present a problem to those operating for this condition.

The second stage of hypospadias repair is the formation of a urethra. Davis has reported good results with his tube or pedicle flap. Byars successfully treated 60 cases by his use of a local skin flap. McIndoe, confining his surgery to older children and adults with the use of a free thin graft and indwelling dilators, reported good results. Young and Benjamin, modifying the operation of Nové Josserand, reported 10 cases with primary anastomosis of a free graft with the urethra. Three cases were successful, seven acquired urinary fistulas which were subsequently closed. Havens reported 29 cases operated upon by the method of McIndoe with 27 good results, one fair and one a failure. We believe that complete correction should be performed in the preschool age if possible.

Almost all procedures designed, irrespective of the basic principle, create a distal urethra without anastomosis to the proximal portion. This is left for a third stage operation. It is not true in the technique advocated by Young and Benjamin who performed primary anastomosis of a free graft with the proximal

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Read at annual meeting of American Urological Association, Pittsburgh, Pa., May 6-9, 1957.

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a search was made to develop a technique to overcome this difficulty This problem has not only been our problem but is mentioned throughout the entire literature

Byars in reporting on his technique for surgical repair of hypospadias states, "The over-all problem of hypospadias repair is such that no scheme regardless of the skill of execution will not be complicated by the occasional development of one or more fistulas even though in most instances proper planning, gentleness of execution, utilization of proper suture material and closure in depth will avoid this complication " David M Davis, in discussing his tube flap operation for repair of hypospadias, states with regard to his method of closing such a fistula "This method is successful in at least two-thirds of the cases on the first attempt and always on the second or third " It is obvious from this that more difficulty with fistulas was encountered than was statistically stated Douglas in recounting his experiences in the operative and postoperative management of hypospadias states, ' Small fistulas are to be expected in any work involving so much suturing of thin and somewhat scarred tissue and in a field which usually is not dry In our series of cases, fistulas have been comparatively few, averaging slightly over one per case "

To our way of thinking, this is not few and more than should occur By means of the free graft using a tunnelization method, only one postoperative fistula can occur and that at the proximal end of the tunnel We were not and are not satisfied with such an incidence of fistula formation This was one of the complications which impelled McCormick to modify the technique of Benjamin and Young

THE PRINCIPLE OF THE THIRD DEGREE

It is conceded that the nearer to the perineum the anastomosis can be accomplished, the easier it is to perform With this principle in mind, it was decided to convert a penile or second degree hypospadias to third degree or scrotal hypospadias (table 1) The first two cases were corrected by moving the urethral meatus back to the scrotum at the time of the chordee repair These openings were near the scrotum and easily transposed For the lesser degrees of hypospadias, a different technique has been devised At the time of the formation of the urethra by a free skin graft, the graft is cut longer than is usually necessary With a sound in the urethra a double barrel urethrostomy is performed in the midscrotal region A free graft about a catheter is then passed through the new meatus at the tip of the glans, subcutaneously in the newly formed tunnel, through the urethra and out the distal opening of the double barreled urethrostomy in the midscrotum The graft extends from beyond the tip of the penis through into the normal urethra No attempt is made to suture the graft to the proximal urethra It is allowed to heal and anastomose itself over the polyethylene tube The tissues over the penile portion of the urethra are then closed in depth with interrupted 0000 chromic catgut (figs 2 and 3) After one week the rubber catheter is removed, leaving the graft in place and a polyethylene tube is

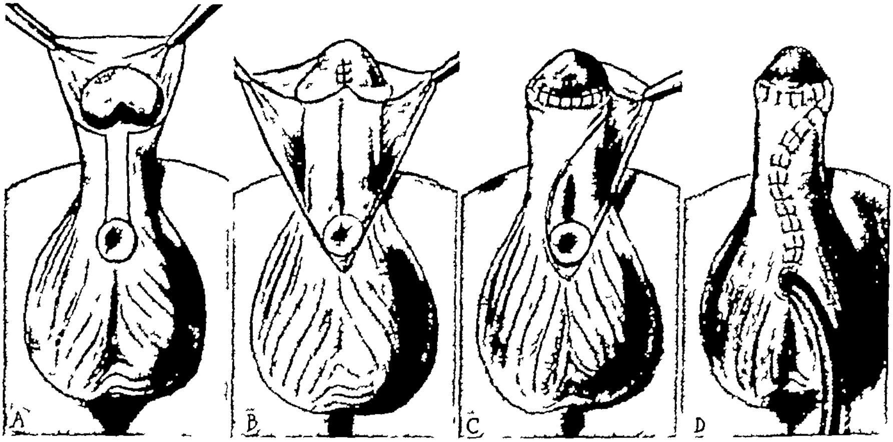

FIG 1 *A*, incisions for correction of chordee Note incision into cleft of glans *B*, note wide lateral exposure of skin flaps Cleft in penis excised and reapproximated All tissue removed down to corpora Urethral meatus freed up to be moved proximally *C*, closure of flap about corona *D*, completion of correction of chordee with Z type closure Foley catheter in place

urethra at the time of implantation McCormick, who has also modified this operation, states that, "This procedure has worked very satisfactorily for the construction of a urethra to the point of the anastomosis but has given a considerable percentage of complications at the anastomotic site These complications have been two first, the development of a postoperative single fistula at the site of the anastomosis, and secondly, the development of a temporary contracture at the anastomotic site which required careful observation and periodic dilatation "

Experience with our early cases resulted in just these complications and forced us to seek an answer to our problem Of 21 cases treated by free skin grafts, six had immediate anastomosis and in all, fistulas developed All required periodic dilatation Three are successfully closed and voiding well but three still have fistulas McIndoe in dealing with thin skin grafts first recommended and used an indwelling dilator This had to be changed frequently and cleansed In 17 cases we have not performed primary anastomosis In these we have used a permanent dilator of polyethylene tubing from a transfusion apparatus formed as a continuous loop in the graft This has been left in for periods of six months to a year without changing and without any reaction or discharge about the grafted urethra The new urethra has shown no tendency to contract after this period of time Children ranged in ages from two years to eleven years and no problem has yet presented itself from the presence of the tube in the new urethra Without this inlying dilator some degree of contracture will occur even though the rate may be only 10 to 25 per cent as predicted by McCormick

The third phase of the reconstruction, namely, the anastomosing of the new urethra with the proximal urethra has presented us our biggest problem In six cases fistulas developed, three were closed in one attempt and three still have small fistulous openings It was felt that these results were less than optimal and

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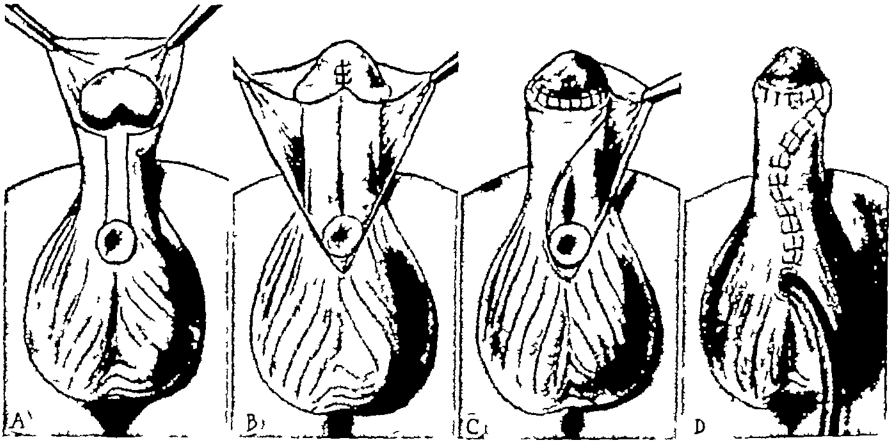

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The third phase of the reconstruction, *namely, the anastomosing of the new* urethra with the proximal urethra has presented us our biggest problem In six cases fistulas developed, three were closed in one attempt and three still have small fistulous openings It was felt that these results were less than optimal and

a search was made to develop a technique to overcome this difficulty This problem has not only been our problem but is mentioned throughout the entire literature

Byars in reporting on his technique for surgical repair of hypospadias states, "The over-all problem of hypospadias repair is such that no scheme regardless of the skill of execution will not be complicated by the occasional development of one or more fistulas even though in most instances proper planning, gentleness of execution, utilization of proper suture material and closure in depth will avoid this complication " David M Davis, in discussing his tube flap operation for repair of hypospadias, states with regard to his method of closing such a fistula "This method is successful in at least two-thirds of the cases on the first attempt and always on the second or third " It is obvious from this that more difficulty with fistulas was encountered than was statistically stated Douglas in recounting his experiences in the operative and postoperative management of hypospadias states, "Small fistulas are to be expected in any work involving so much suturing of thin and somewhat scarred tissue and in a field which usually is not dry In our series of cases, fistulas have been comparatively few, averaging slightly over one per case "

To our way of thinking, this is not few and more than should occur By means of the free graft using a tunnelization method, only one postoperative fistula can occur and that at the proximal end of the tunnel We were not and are not satisfied with such an incidence of fistula formation This was one of the complications which impelled McCormick to modify the technique of Benjamin and Young

THE PRINCIPLE OF THE THIRD DEGREE

It is conceded that the nearer to the perineum the anastomosis can be accomplished, the easier it is to perform With this principle in mind, it was decided to convert a penile or second degree hypospadias to third degree or scrotal hypospadias (table 1) The first two cases were corrected by moving the urethral meatus back to the scrotum at the time of the chordee repair These openings were near the scrotum and easily transposed For the lesser degrees of hypospadias, a different technique has been devised At the time of the formation of the urethra by a free skin graft, the graft is cut longer than is usually necessary With a sound in the urethra a double barrel urethrostomy is performed in the midscrotal region A free graft about a catheter is then passed through the new meatus at the tip of the glans, subcutaneously in the newly formed tunnel, through the urethra and out the distal opening of the double barreled urethrostomy in the midscrotum The graft extends from beyond the tip of the penis through into the normal urethra No attempt is made to suture the graft to the proximal urethra It is allowed to heal and anastomose itself over the polyethylene tube The tissues over the penile portion of the urethra are then closed in depth with interrupted 0000 chromic catgut (figs 2 and 3) After one week the rubber catheter is removed, leaving the graft in place and a polyethylene tube is

TABLE 1 *Plan of operation*

- I Correction of chordee (age—after 2 years)
  - A) Sutures 0000 chromic, No 35 stainless steel wire
  - B) Dressing Elastoplast, penis free, not sewn to abdomen
- II Formation of urethra
  - A) Time interval 6 months or more
  - B) Free graft
    - 1) Site inner side of arm
    - 2) Thickness 15–22 thousandths of inch (depends on age of patient)
    - 3) Secured about 14F rubber catheter, fixed with plastic cement (dermatome)
    - 4) Graft passed through tunnel from tip of glans to urethra, through urethra to double barreled scrotal urethrostomy
    - 5) Urine diverted through proximal opening of urethrostomy
    - 6) Sutures 0000 chromic catgut
    - 7) No dressing
  - C) Polyethylene tubing
    - Rubber catheter, removed on 7th or 8th day, replaced by polyethylene tube
- III Closure of double barreled scrotal urethrostomy
  - A) Time interval 6 months or more
  - B) Urine diverted by perineal urethrostomy or Foley catheter
  - C) Closure
    - 1) Interrupted inverting sutures
    - 2) Fascia 0000 chromic catgut
    - 3) Skin silk or chromic catgut
    - 4) No dressing

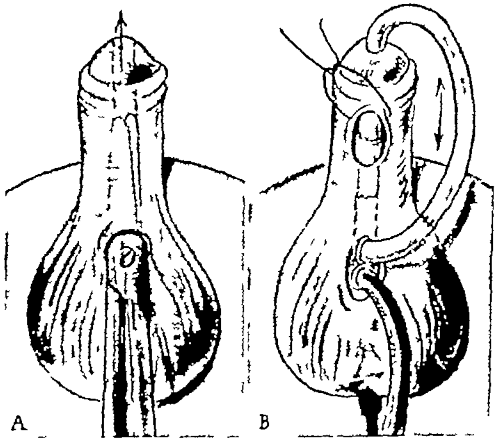

FIG 2 A, tunnelling with dissecting scissors to tip of glans *B*, composite drawing shows free graft passing from tip of glans into normal urethra Polyethylene tube in place through double barrel scrotal urethrostomy Closure of opening on penis begun Urine diverted by Foley catheter

inserted The ends of the tubing are sewed together to form an external loop In the immediate postoperative period diversion of the urinary stream is accomplished through the proximal portion of the double barreled urethrostomy Six months later the third stage is completed utilizing a perineal urethrostomy or

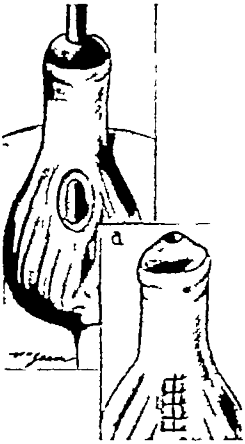

FIG 3 Closure of scrotal urethrostomy over Foley catheter Note depth of tissue Insert (a) shows final closure

TABLE 2

Total number of cases—29
Type of operation
  1) Free graft—21
  2) Other methods—8
Modifications of free graft
  1) Primary anastomosis—6
    a) Fistula—6
    b) Healed and complete—3
    c) To be completed—3
  2) Delayed anastomosis—15
    a) Fistula—6
      1) Closed first attempt—3
      2) With fistula—3
    c) Unfinished—4
    d) Converted to third degree or scrotal hypospadias
      1) By moving back meatus
        a) Two closed no fistula
      2) By long graft to scrotum
        a) Three closed
          2—no fistula at scrotum
          2—no fistula on penis
          1—tiny fistula on penis
          1—tiny fistula at scrotum

Foley catheter per urethram for urinary diversion The double barreled scrotal urethrostomy is closed in layers using an inverting interrupted suture on the urethra and closing the tissue in depth with interrupted 0000 chromic catgut Three cases have now been completed successfully by this method

Our results are cited in table 2

Figures 4, 5 and 6 are illustrative cases

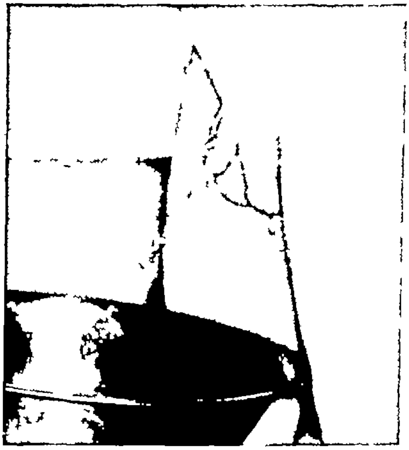

Fig 4 P D , No 112951 Patient voiding, final result Free graft with primary anastomosis required dilatation of the urethra

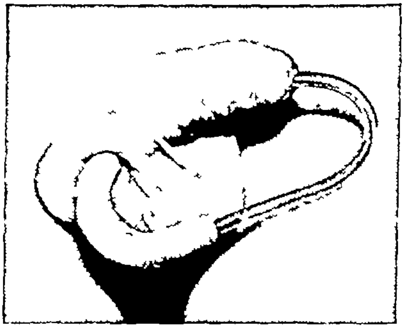

Fig 5 D M , No 164143 Polyethylene tube in place in penile hypospadias treated by principle of third degree Tube is shown coming out of tip of penis and scrotal urethrostomy Original opening on shaft of penis closed It can be detected by scarring present in skin

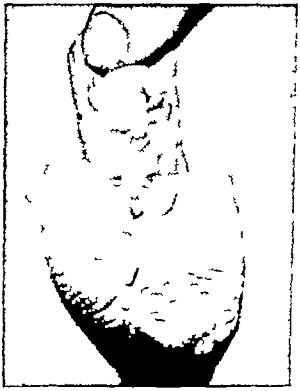

Fig 6 C C , No 187187 Final result after closure in scrotum (principle of third degree) Patient was referred after two attempts at correction of chordee by general surgeon Extensive scarring would preclude use of local skin flap

DISCUSSION

We believe that the repair of hypospadias should be performed in three stages Correction of the chordee should be accomplished at an early age preferably between one and three years This allows adequate growth of the penis The free skin graft appears to grow clinically as the patients grow, and therefore offers no contraindication to its use in the young Many authors advocate delay until the early teens before operative repair because the patients have not had psychological difficulties and have made good adjustments to their problem These surely must be superficial clinical observations as no one has reported psychological or psychiatric evaluation of a group of unrepaired hypospadias To us it is significant that invariably the parents will voluntarily report marked improvement in the child's social adjustment, decrease in difficulties of management of the child, and a noticeable increase in aggressiveness

While the repair of the chordee is a time-consuming, meticulous procedure, the second and third stages are usually easily and rapidly performed, rarely taking more than one half to three quarters of an hour The plastic polyethylene tube in place has not presented a problem In one instance the tube accidently came out and was replaced the next day without difficulty No discharge or irritation has occurred around the tube The mother is instructed to move the tube forward and backward occasionally and to use a lubricant locally if it fails to move with ease The caliber of this polyethylene tube is approximately that of a 14F sound and provides a urethra with a very adequate caliber McCormick reported an operation for simultaneous repair of the chordee and implantation of the graft in one stage He reported three cases successfully treated by this method He, too, no longer performs a primary anastomosis of the graft and the urethra but he does this at a later date preferrably at least six months after the first stage

The principle of third degree is based on sound surgical principles It allows the closure of the fistula to be performed in an area of essentially normal tissues, permits the closure of several layers in depth over the opening in the urethra, and it contributes to an accurate and non-strictured anastomosis in a dry field over a period of six months

This plan of hypospadias repair creates a penis which 1) is normal in appearance, 2) has a nearly normal redundant foreskin, 3) has the urethral meatus at the tip of the glans where it belongs, and 4) does not have scar tissue in the urethra

SUMMARY

We believe that to our satisfaction the first two problems in the repair of hypospadias have been solved 1) the adequate correction of the chordee and 2) the formation of an adequate urethra without scarring or contracture

The third and final problem of fistula formation seems to respond well to the principle of the third degree One may be assured that irrespective of an [illegible] of repair some percentage of fistula will occur

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A 10-YEAR-OLD BOY WITH A POSITIVE SEX CHROMATIN TEST

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From the Departments of Urology and Obstetrics and Gynecology, Medical School, State University of Iowa, Iowa City, Iowa

D B, a 10-year-old white boy, was referred by Dr Frederick C Brush of Mason City, Iowa, because the mother believed the boy's genitalia were not developing at a normal rate

The patient was the second oldest of five children and all of the siblings were considered normal by their parents The mother stated this boy was born 10 days prematurely, and weighed 7 pounds 13 ounces and was 21 inches long He walked at the age of 14 months and other developmental attainments very closely approximated those of an older brother At the age of 8½ years, Dr Brush examined the child and judged the genitalia were slightly below the expected normal size A course of chorionic gonadotrophin, 500 units twice a week for three weeks, was given and the penis became slightly larger but no increase in testicular size was noted Six months later the course was repeated, again only a slight penile enlargement was noted The size of the genitalia then remained unchanged to the time of consultation at the University Hospitals

On physical examination the patient appeared to be a healthy, alert, slightly obese boy of 10 years Height, 5 feet, weight, 110 pounds (fig 1) Examination of the head was negative The lungs were clear to auscultation and percussion The heart was not enlarged and no murmurs were heard The blood pressure was 110/75 mm Hg The abdomen was normal The penis was 3 8 cm in length and 1 7 cm in diameter The testes were not unusual in size, consistency and sensitivity (fig 2) The prostate was barely palpable per rectum

The urine was negative both chemically and microscopically The hemoglobin was 12 gm per 100 ml The white blood cell count was 6,500 per cu mm Two 24-hour urine samples contained 3 8 and 3 9 mg of 17-ketosteroids per gram of urinary creatinine These are normal juvenile values No gonadotrophic hormone was detected in 12-hour aliquots of the first specimen but the second specimen obtained postoperatively had gonadotrophin of the L H type in similar aliquots An x-ray film of the right wrist was interpreted as corresponding to the expected bone development at age of 10 years

It was the impression of the examining physician and several others that the patient was just a normal boy However, an oral smear was obtained and 46 per cent of the cells counted contained the sex chromatin body (female type) Consequently, under general anesthesia, the scrotal contents were delivered through surgical incisions and the left gonad measured 1 5 by 1 0 cm and the right gonad measured 1 4 by 0 9 cm Both vasa deferentia and epididymides were present On incision, the parenchyma of the gonads was yellow in color, did not string and appeared to the surgeon much like that seen in Klinefelter's

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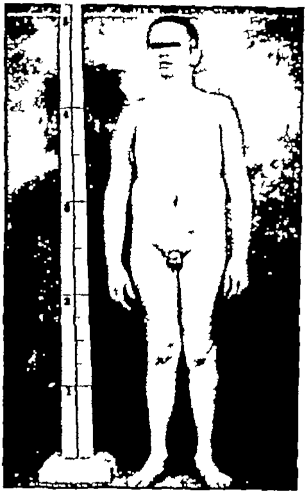

FIG 1 Patient aged 10 years

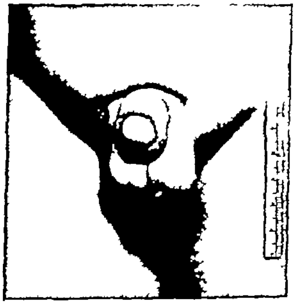

FIG 2 Genitalia

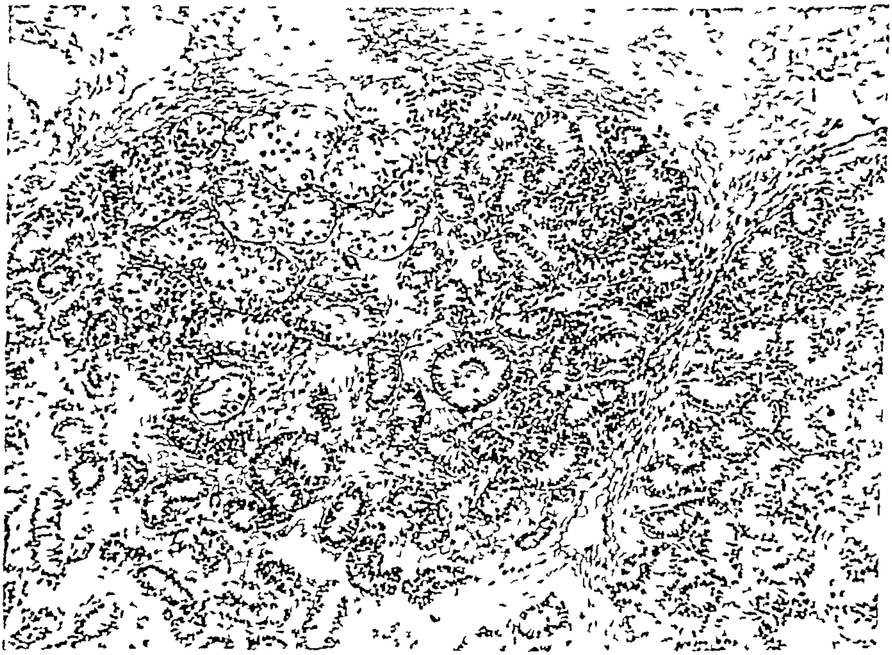

FIG 3 Section of gonad Low power Tunica vaginalis at top border of picture Convoluted tubules in right half of field are sterile Larger convoluted tubule at upper left contains many germ cells Intratubular egg about center H & E

syndrome Small wedges were removed for histological examination The tunica was closed with catgut and the testes replaced in the scrotum

Gonadal histology The tunica albuginea is well developed The septula are continuous with the tunica vasculosa and divide the parenchyma into lobules (fig 3) The interstitial spaces contain capillaries and scattered connective tissue cells *All convoluted tubules are lined with sustentacular cells, have a basement* membrane and a thin lamellated connective tissue wall Some tubules are larger and contain, in addition, germ cells with large spherical nuclei and abundant cytoplasm (fig 4) No progressive stages of spermatogenesis are present Mitotic activity is not evident in germ cells but several contain tetrads Some of the larger germ cells are invested in a single layer of sustentacular cells

Occasionally a tubule has a dilated portion which contains an egg-like body surrounded by a second layer of sustentacular cells (figs 5 and 6) These ovular bodies are 60 to 120 microns in diameter and have a nuclear area which stains

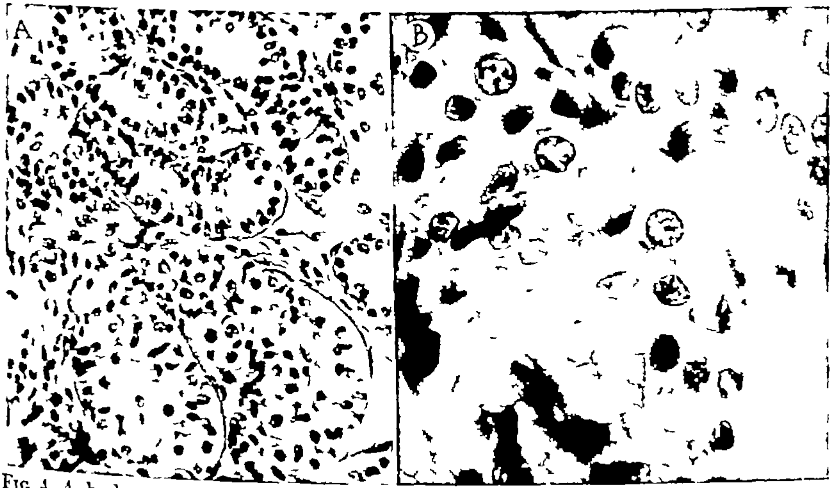

Fig 4 *A*, high power Midportion of figure 3 adjacent to tunica vaginalis taken to show sterile tubule, above, in contrast to one with germ cells, below *B*, oil immersion detail of germ cells within convoluted tubule Granular elements in cytoplasm were glycogen (Schiff positive elements that were removed by saliva) One cell is binucleate

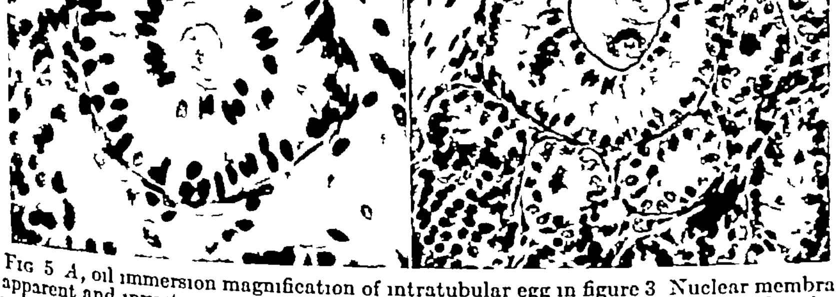

Fig 5 *A*, oil immersion magnification of intratubular egg in figure 3 Nuclear membrane is apparent and investing sustentacular cells give appearance of corona radiata *B* oil immersion detail PAS positive crescentic body and large vacuole in ovum Deep staining periphery Deep staining clumps of nuclei between two layers of sustentacular cells and also in adjacent tubule

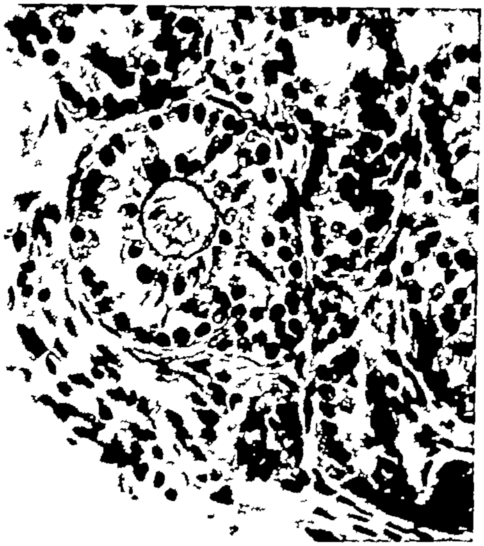

FIG 6 Oil immersion of H & E preparation Diffusely staining nuclear area Continuation of tubule is shown at lower right side of dilated portion

diffusely with hematoxylin, intensely with periodic acid, Schiff (PAS) and exhibits metachromasia with toluidine blue The cytoplasmic portion stains lightly with eosin, may be vacuolated or laminated and peripherally may stain deeply with PAS

Darkly staining clumps of cells, possibly exhibiting plasmogamy occur in some tubules (fig 5, *B*) Certain connective tissue septa contain cords of deep staining cells which are continuous with some of the convoluted tubules These cords have no basement membrane or lamellated connective tissue wall The cells contain very deeply staining spindle-shaped nuclei and scant cytoplasm It is not obvious whether these cords represent undifferentiated or degenerating tubules but several small egg-like bodies were seen in these cords

DISCUSSION

Since the only known instances of sex chromatin-positive "males" have been cases of the postpubertal syndrome of Klinefelter,[1] [4] there is strong presumptive evidence that the syndrome will ultimately develop in this boy A previous communication[5] attempted to resolve the paradox of genetic femaleness (positive chromatin findings) in patients with histologic evidence of maleness (spermatogenesis) A working hypothesis was presented suggesting that the syndrome results from bilateral failure of the embryonic ovarian cortex and persistence of the ovarian medulla Biopsy of the gonads of this prepubertal chromatin positive boy afforded an opportunity to search for possible evidence of femaleness The intratubular bodies have been considered as ova because 1) they have a nucleus, 2) of the large size and the abundant albuminous cytoplasm, 3) the outermost zone on the cytoplasm stains like a zona pellucida, 4) the radial arrangement of the investing sustentacular cells resembles a corona radiata, 5) oocytes have been described in the seminal tubules of hermaphroditic sexually immature animals[4] Recently we found identical oocytes in the tubules of the right undescended testis of a chromatin-negative hypospadiac six-year-old boy whose left lower abdomen contained a fallopian tube and an undifferentiated gonad (seminoma) Since intratubular oocytes may occur in either chromatin positive or negative individuals it is evident that the chromatin test may not predict the histologic nature of the gonads in sexually abnormal individuals Indeed patients with ovotestes may be either chromatin positive or negative[4]

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The Klinefelter's syndrome is the adult manifestation of a "true intersex" if this ten year old patient and other similar cases develop the syndrome

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PROBLEMS ENCOUNTERED IN THE TREATMENT OF PROSTATISM

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To the author, the subject of prostatism is of special interest because the treatment of this purely sexual gland has been largely responsible for the separation of urology as a specialty from general surgery. Not only did the urologist demonstrate to the general surgeon that he could handle diseases of the prostate much better, but he impressed upon the surgeon the importance of a careful urological survey and the proper preparation of a case before operation.

The condition of prostatism, no doubt, has been suffered by the same percentage of elderly men since time immemorial, or at least since the time at which men lived sufficiently long to enter the so-called prostatic age. Not until about the middle of the sixteenth century was the prostate gland considered the cause of obstruction at the neck of the bladder. This discovery was attributed to Nicolo Ulassa, a Venetian physician. Following the discovery of the gland and the knowledge that enlargement caused obstruction at the vesical neck, methods of treating this condition up to the time of the strictly surgical era, consisted for the most part of tunneling through the gland as practiced by John Hunter. Very little progress was made in the treatment of prostatic obstruction until the middle of the eighteenth century when surgical procedures were instituted for removal of stones from the bladder. Such men as Sir Henry Thompson, Gouley, Desault, Guthrie, Mercier and Sir William Blizzard played a prominent part in the evolution of the management of this condition through the pre-surgical years.

It appears that the modern surgical procedures for removal of the prostate gland are the ultimate results of perineal lithotomy for stone. Belfield must be considered one of the pioneers of modern surgery of the prostate gland. It is probable that perineal prostatectomy preceded the suprapubic operation by several years. Deaver stated that it was employed first for malignant disease by Billroth in 1867. Little progress was made in the perineal operation for the removal of the obstruction at the vesical neck until Goodfellow in 1891 performed perineal enucleation of the lateral lobes with removal of the median lobe. Young, in 1903, described his perineal operation, which has endured in principle, with certain modifications made by himself, Hinman, Geraghty, Lowsley and others, up until the present time.

To Fuller, it seems, belongs the credit for first accomplishing not only the removal of the intravesical enlargement of the prostate gland but the intraurethral enlargement as well, by the process of suprapubic enucleation. Freyer of England claimed in 1900 priority for the method of total enucleation suprapubically of the hypertrophied prostate, but according to Fuller, it was brought to Freyer's attention in the same year by Guiteras, who explained to Freyer his own and

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Read at a meeting of the New York Section of the American Urological Association in New York City, November 21, 1956.

Fuller's technique at that time J Bentley Squier and J W Thomson-Walker further modified Fuller's and Freyer's technique for suprapubic prostatectomy and since then, there have been various modifications by different men too numerous to mention

In regard to transurethral surgery, Guthrie, in 1834, described a prostatic catheter which enclosed a blade that could be projected from within the instrument that cut the bar as the instrument was passed into the bladder Methods of reducing the size of the prostate gland by use of the galvanocautery were introduced about 1873 with the Bottini operation A few of the more prominent men who have played a part in the further development of transurethral prostatic resection are Chetwood, Young, Caulk, Collings, Stern, Alcock, Braasch, McCarthy, Kirwin, Theodore M Davis, Nesbit and G J Thompson

It might be of interest to review the management of prostatism over the past 43 years, during which time the author has had the opportunity of observing the methods of handling this disease, including various changes in operative technique and the pitfalls which one may encounter as a urological surgeon Malignancy of the prostate will be eliminated from this paper, as this condition, by its very nature, is fraught with more complications than is prostatism arising from benign enlargement

Graduation from the University of Pennsylvania Medical School was in 1913 No operation on the prostate was done before the class during the four-year period The author's initiation in the treatment of this disease was in the first two months of internship At that time, practically all prostatic surgery, in and about Philadelphia, was handled by the general surgeon It was very difficult then, as it is now, to obtain accurate information regarding mortality and morbidity, but as some of you may recall, it was extremely high—probably 50 per cent or more In those days, no preparation of the patient was considered important He was admitted to the hospital in retention, he was promptly operated upon and the following day or so, ready for the tender care of the undertaker

Young was probably one of the first to observe the benefits described from preliminary drainage of the bladder In 1899, in a case in which there was deep uremic coma and a hugely distended bladder, catheterization was attempted without success and suprapubic drainage was carried out Young witnessed the amazing disappearance of the coma and restoration of an apparently normal condition as a result of drainage One month later, Young carried out his first suprapubic prostatectomy, removing a huge prostate gland successfully through the previous cystotomy incision This was the first recorded two stage suprapubic prostatectomy

Deming and Axilrod compared a group of 100 patients admitted to the New Haven Hospital for the treatment of prostatism from 1878 to 1908, with a second group of 100 cases admitted over a period of nine months, from December 6, 1947 to September 5, 1948 The operative mortality in the first group was 32 per cent The morbidity was extremely high as the records show that only 3 cases operated upon were discharged from the hospital as well The mortality rate in the second group was 4 per cent This included perineal, transurethral, retropubic and suprapubic surgery and malignant prostates as well as benign. Of this group 96 per cent were entirely relieved of obstruction against 8 per cent of the early series. Even if these latter figures represent only the condition of the patients at the time of their discharge from the hospital, it demonstrates the marked advancement that has been made in the treatment of prostatism.

The patient who consults the urologist today for relief of distressing symptoms of prostatism expects and is entitled to a good functional postoperative result. If residual prostatic tissue is left behind, associated with infection, or traumatic strictures from injury to the urethra, the patient may be worse off in many cases than if surgery had been omitted. We all agree that the present day urologist should be well trained in the four surgical procedures for the removal of the prostate gland and select the operation which is best suited for the individual case, rather than to fit the case into one type of operation. However, this is not true in the majority of instances because the average urologist will perfect one technique over another and will use the one in which he feels he is most capable of performing, and sometimes is apt to recommend the operation which appeals to the patient and to the referring physician as a more minor procedure with a shorter hospital stay. This is important from an economic standpoint for the average individual, although the various medical-surgical plans throughout the states aid to a large extent. However, we feel we owe our patient a permanent rather than a temporary result and if it is necessary for him to return for treatment of a stricture or the removal of residual tissue, associated with infection, the time gained by the shorter stay in the hospital is hardly worthwhile.

It was shown in our statistical survey on prolonged morbidity following prostatic surgery, published in 1948, that the most popular operation of all was transurethral prostatic resection. That was a report on 14,865 operations with a mortality rate of 3 per cent and a total morbidity of 8.4 per cent. Of the suprapubic operations, the two-stage procedure showed a 4.8 per cent morbidity in comparison to the 11.6 per cent morbidity in the one-stage operation. Perineal operations showed a morbidity of 5.9 per cent, single resections a morbidity of 8.4 per cent and multiple resections, 10.9 per cent. The lowest morbidity was following the two-stage suprapubic prostatectomy. As of today, we can be proud of our low mortality, but should we be satisfied with the morbidity, as it is reasonable to assume that these represent minimal figures, since many patients do not return to the original surgeon when complications persist or arise. We should all strive to reduce the morbidity, which, in the author's opinion, is still too high. Our aim should be comfort in voiding for the remainder of the patient's life, provided malignancy does not develop.

We still adhere, more or less, to our method of selecting cases for operation, published in 1937, under the heading of "New Methods of Preoperative Study in Prostatic Hyperplasia," in which we recommend a most careful medical and urological survey of the case, with intraurethral and intravesical cystoscopic grading (unless contraindicated), and grouping of these cases for operation according to the findings. In selecting cases for transurethral resection, we include those with a contracted vesical outlet, fibrous bar or small middle lobe, avoiding the intraurethral and large vascular subcervical glandular hyperplasias At the present time, we have a number of outstanding "resectionists" in this country who do a magnificent job and can handle most any type of enlargement, but the author has not had the opportunity of seeing any of their cases because where good results are obtained, it is not necessary for the patient to consult another physician On the other hand, among those cases that have come under our observation from various sections of the country, we have noted the following That where attempts have been made to resect large prostates, especially the intraurethral lateral lobes, there still remains residual tissue, with few exceptions This often means persistent pyuria, because the remaining portion of the hyperplastic tissue has been largely deprived of its blood supply These patients may or may not have residual urine, but the symptoms of prostatism persist Probably one of the frequent complications following transurethral resection is stricture which has been attributed, by a number of men, to the use of the inlying catheter with subsequent infection However, we feel as most of these strictures can be classified as traumatic, they are due to the lack of preparation of the urethra, in the form of dilatation and meatotomy, to receive the resectoscope, and the back and forward motion of the instrument with the generation of heat in an improperly lubricated urethra These strictures are most commonly found at the meatus and in the penile-scrotal portion of the anterior urethra At the present time, we have a number of cases with extensive traumatic strictures following transurethral resection which will probably require a lifetime of treatment in the form of dilatation, as operation for the correction of a stricture in this location is frequently unsuccessful

It is our opinion that where the meatus is small, a meatotomy should be performed, and, in doing so, the cut margin of the mucosa and glans penis should be brought together by interrupted plain fine catgut sutures Any other narrowing of the urethra, whether physiological or organic, should be dilated a sufficient time before operation to allow the passage of a 30F sound to the bladder with ease, provided that a 28F resectoscope is to be used for the operation In cases with a short penile ligament and small caliber urethra, it is best to do an external urethrotomy and to enter the bladder from the bulb, as recommended by Nesbit, however, where a transurethral resection is the operation of choice, we prefer in such cases, a transvesical approach, and if contraction of the bladder neck or bar is present, sharp dissection with repair

In the early and mid-twenties, the author had the opportunity of spending some time with Sir John Thomson-Walker and observing at first hand, his technique of suprapubic prostatectomy In 1919, Sir John presented his ideas of the causes for postoperative obstruction and his own operation for its prevention He stressed two danger points for the development of stricture after suprapubic prostatectomy namely at the membranous urethra where the mucous membrane is severed, and at the outlet of the bladder, where the mucosa of the neck of the bladder is torn across He stated there was little tendency to contraction at the membranous urethra in the presence of an inlying catheter or intermittent catheterization, but at the entrance from the prostatic cavity into the bladder the danger is greater It has been the observation of many surgeo that closure of the internal urethral orifice or marked narrowing has occurre as the result of cohesion of irregular tags and flaps of mucous membrane th have previously overlain the intravesical portion of the gland and which ha been torn in the enucleation, with the formation of a diaphragm separating th prostatic cavity from the bladder His operation was presented to prevent suc obstruction by cutting a wedge shaped piece of tissue from the fold lying at th posterior lip of the prostatovesical opening and the control of hemorrhage, b suture, as previously advocated by Judd and Cabot We still follow the techniq of this operation in a modified form

Goldstein and Rubin reported on 3 cases of complete occlusion of the vesic orifice following suprapubic prostatectomy and quoted Thomson-Walker on th method of preventing this complication They further state that a review of th literature reveals that occlusions have only occurred at the vesical orifice W have observed one case in which complete obstruction occurred at the junctio of the apex of the prostate and membranous urethra, due, we feel, principally t the fact that an inlying catheter was not used following surgery nor was the any dilatation of the urethra or intermittent catheterization We have not e perienced any stricture at the location aforementioned since carrying out th technique

Following enucleation, one should carefully inspect the prostatovesical outle This is probably more adequately accomplished in retropubic surgery, howeve if one has been well trained in suprapubic technique, there is no difficulty in r pairing the vesical outlet following a one-stage operation, except in very obe individuals

The prostate, in addition to its intrusion into the urethral lumen, enlarges i two directions, namely, into the bladder through the lumen of the vesical sphincte or below the base of the bladder, so-called subvesical type of hyperplasia I the latter, following enucleation, unless a small V shaped piece is excised fro the apex of the trigone, there exists at the posterior lip of the vesical outlet shelf with a depressed area below This does not interfere with voiding, but i sometimes makes the introduction of a catheter difficult, unless one elevates th tip with a finger in the rectum, as it enters the bladder cavity

We are still old-fashioned enough to use the two-stage suprapubic prostatectomy for cases in which we feel this procedure is indicated Ours was one of th first clinics to emphasize the importance of excretory urography in the preoperative study of the upper urinary tract in the presence of obstruction at the vesica outlet We still find this procedure most valuable, as not infrequently one encounters unilateral renal disease in cases that would pass unnoticed with the usua routine studies Knowing that definite disease exists in the upper urinary tract the surgeon may select the operation best suited for the patient However, sinc the advent of chemotherapy and antibiotics, we have become bolder in the handling of such cases

We would like to emphasize the danger of forcefully using the fingers or forceps in removing the mobilized gland from the prostatic cavity, as frequentl tags of mucous membrane remain adherent to the apex and base of the hyperplastic tissue, and if forcibly removed, may injure the membranous urethra and tear the mucosa at the base of the bladder. Attachments of the mucosa to the prostate, following mobilization, should be severed by sharp dissection under direct vision. If this is not possible, then by the sense of touch, using long, blunt pointed, curved scissors, as injury to the membranous urethra may lead to incontinence and that of the bladder, to prolong bleeding unless repaired.

The fear of hemorrhage following prostatic surgery has brought forth many suggestions for its control. In the early days, we were particularly concerned about postoperative bleeding because of our inability to replace the blood loss and packing of the prostatic cavity was a common procedure. This packing was generally removed within 48 to 72 hours. The presence of the foreign body produced severe bladder spasm which required, in many instances, heavy sedation. There is always some infection of the bladder and prostatic cavity following surgery, however, in the old days, as the result of prolonged pressure from gauze packing, interfering with the blood supply to the vesical neck and prostate, the infection was much more severe and frequently involved the upper urinary tract. We now feel that prolonged pressure, by gauze packing or bag hemostasis following enucleation of the gland, not only increases infection, but may be a factor in causing excessive bleeding by preventing the normal contracture of the vesical neck and the prostatic capsule, as they have an abundance of smooth muscle which, like all smooth muscle, possesses the inherent properties of tonicity and resistance to extension.

In the twenties, when the author was visiting Dr. Edmund Papin's clinic in Paris, France, he noted that following enucleation of the prostate gland nothing was placed in the prostatic cavity. A Marion tube was used for suprapubic drainage and bladder irrigation. At that time we were most concerned about postoperative hemorrhage and inquired of the clinic why some means of hemostasis was not utilized. The reply was, "The patient seldom, if ever, bleeds to death and that nature contracts the vesical neck and prostatic capsule, following enucleation of the gland, similar to the contraction of the uterus following delivery of the placenta." It took a number of years for us to be convinced that this was true in the majority of cases and that any bag or packing placed in the prostatic cavity, following enucleation was a mistake; however, we must admit that there are exceptional cases where such a procedure is necessary. It is our present opinion that if any enlarged prostate is properly enucleated, with control of the major arterial bleeding at the operating table, the contracture of the vesical neck and prostatic capsule will take care of the rest and that keeping the prostatic fossa dilated may cause excessive hemorrhage.

We have used most of the methods recommended for the control of hemorrhage. For many years the Pilcher bag was our procedure of choice, and then the Pilcher bag surrounded by gelfoam or oxidized cellulose. Gelfoam caused a lot of trouble in the form of postoperative obstruction which required removal before the patient could void, so these have long since been discontinued. At the present time, a 22F Foley catheter with a 30 cc bag capacity, is placed in the bladder and the bladder the danger is greater It has been the observation of many surgeons that closure of the internal urethral orifice or marked narrowing has occurred as the result of cohesion of irregular tags and flaps of mucous membrane that have previously overlain the intravesical portion of the gland and which have been torn in the enucleation, with the formation of a diaphragm separating the prostatic cavity from the bladder His operation was presented to prevent such obstruction by cutting a wedge shaped piece of tissue from the fold lying at the posterior lip of the prostatovesical opening and the control of hemorrhage, by suture, as previously advocated by Judd and Cabot We still follow the technique of this operation in a modified form

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We would like to emphasize the danger of forcefully using the fingers or forceps in removing the mobilized gland from the prostatic cavity, as frequently

It was formerly customary for us, following prostatic surgery, to irrigate the bladder frequently to clear up residual infection, and to cystoscope the patient before discharge to determine the result of the procedure At present, we feel the less one does in the average case, following surgery, the better off the patient will be The author can well remember in reading a paper on prostatism, before the New Jersey State Medical Society in 1930, the comments made by the late Stanley R Woodruff of Jersey City, who said in part "My own individual experience with patients is that I do not like to fuss with them after operation " It took us sometime to agree with this statement, however, there are certain cases, regardless of the type of procedure which is used, that require some postoperative treatment, but the majority respond to internal medication alone, provided the operation has been properly accomplished If one is concerned about the possibility of residual urine, it can easily be determined by excretory urography, with a film taken before and after voiding

In closing, we would like to emphasize that the same care should be used in the selection of cases for operation on the prostate as we did prior to the advent of chemotherapy and antibiotics and that in prostatic hyperplasia with urinary retention, associated with upper urinary tract lesions, whether unilateral or bilateral, and cardiovascular disease, drainage is an important factor, regardless of the technique used for the removal of the obstruction, and that the improvement in the patient's general condition is often in direct proportion to the type and duration of such drainage In this fast moving world, haste is often resorted to, but more time and proper evaluation of the patient's condition might attain for us more permanent results

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CYTOCHEMICAL STUDIES OF PROSTATIC EPITHELIUM I THE DESOXYRIBOSE NUCLEIC (DNA) CONTENT IN INDIVIDUAL CELLS

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Prostatic disease, both benign and malignant, still remains obscure as to etiology and pathogenesis Frequently, the management of questionable neoplastic areas in otherwise benign enlargement, the so-called occult carcinoma, is indeterminate or delayed, because of the surgeon's inability to resolve the problem of the innate biological potential of such areas Often the true nature of nodules which, because of size, appear favorable for total prostatectomy, cannot be determined because of the difficulties which the pathologist encounters in differentiating between benign and malignant lesions by standard histological techniques Although various pathologists have attempted to establish specific microscopic criteria for a reliable diagnosis, the problem is by no means solved because "the characteristics of malignant cells in general are notoriously absent in many types of prostatic carcinoma "[1] Apparently, the routine microscopical histological examination is not sufficient, but the use of additional methods seems desirable for furthering the differential diagnosis

One approach to the problem which has been very fruitful in elucidating pathogenesis in other diseases, and which seemed promising for this special problem, is concerned with the behavior of the *chemical components* of epithelial cells from normal, hypertrophic, hyperplastic and malignant glands

Since the classical research of Miescher[2] and Kossel[3] established that the nucleoproteins, salt-like compounds of nucleic acid and proteins, are the most important chemical constituents of all the cells, great advances have been made in our understanding of their role in cell growth and metabolism It has now been determined that there are two types of nucleic acid in each cell, the desoxyribose nucleic acid (DNA) which is found in all nuclei and is an integral part of chromosomal material,[4] and the ribose nucleic acid (RNA) which is contained predominately in the cytoplasm and in nucleoli of all cells Although DNA and RNA

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are chemically very similar their behavior in cell metabolism is strikingly different Normal cells have a characteristic constant amount of DNA[5] which is closely correlated with the chromosomal complement and which is usually independent of the physiological activity of the cell and tissue Furthermore there is strong evidence suggesting that DNA may be an essential part of the genetic material In contrast RNA varies greatly in amount with metabolic activity and is closely linked to protein synthesis in cells

In the present investigation which was started 3 years ago we are concerned with the possible changes in the DNA content of epithelial cells from normal and pathological prostatic tissues The analysis of DNA seemed of special significance since previous studies on a variety of human tumors by Leuchtenberger Leuchtenberger and Davis[5] showed that *tumor* cells have an increased DNA content and exhibit a great variability of the DNA amount while cells from various normal human tissues exhibit a striking constancy of the DNA

For this investigation microspectrophotometric methods seemed especially favorable because of the possibility of making quantitative analyses of these important chemical constituents in individual cells directly under the microscope These determinations can be carried out in situ in histological sections, thus permitting a direct correlation between the microscopical appearance of the cells and their chemical composition

MATERIALS AND METHODS

The specimens utilized in this report were obtained from the files of the Institute of Pathology, Western Reserve University School of Medicine and from the operating rooms of the University Hospitals of Cleveland A total of 40 cases were examined 13 benign enlargements 25 malignant tumors of the prostate and 2 normals The normal glands were limited in number by the necessity for having uniformity of age in the study population The number of cells in which the DNA determination was carried out was 2 261 Seventy-six nuclei were from normal prostates 625 nuclei from benign glands and 1 560 nuclei from malignant tumors measured

For the determination of DNA Feulgen microspectrophotometry was used The specificity of the Feulgen reaction for DNA and the validity of microspectrophotometric methods for the quantitative analysis of DNA in individual cells have recently been discussed by Leuchtenberger in a chapter entitled Quantitative Determination of DNA in Cells by Feulgen Microspectrophotometry A detailed description of the apparatus and standardized schedules of the techniques involved are also given

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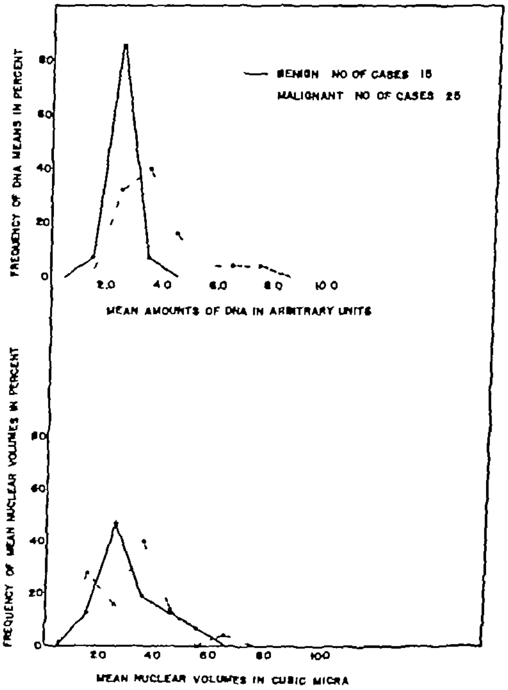
RESULTS

In table 1, the mean DNA values and the mean nuclear volumes for the epithelial cells in 13 benign, two normal, and 25 malignant prostates are presented It is evident from this table that the mean amount of DNA in the two normal prostates is very similar to the mean amount of DNA in the benign lesions All 15 cases show the characteristic and constant diploid amount of DNA found in other normal tissues It can be seen furthermore, that there is very little variation from case to case within the benign group The picture is considerably different if the mean DNA values for the malignant tumors are considered There is not only a considerable number of cases with a much larger amount of DNA than that of the benign and normal ones, but the mean amount of DNA varies considerably from case to case within this group of malignant tumors Comparing the mean nuclear volumes of each group, it can be seen that no significant difference between them is apparent A graphic representation of these data are given in figure 1 Among the 15 benign cases the two normal ones are included It is obvious that the distribution curve for the mean DNA values of the malignant cases shows a wide scatter with a shift to higher values when compared to the narrow range of the mean DNA values for the benign cases It can also be seen



MEAN AMOUNTS OF DNA IN NUCLEI (FEULGEN MICROSPECTROPHOTOMETRY) AND NUCLEAR VOLUMES OF EPITHELIAL CELLS FROM BENIGN HYPERTROPHIC HYPERPLASTIC AND MALIGNANT PROSTATIC GLANDS

FIG 1

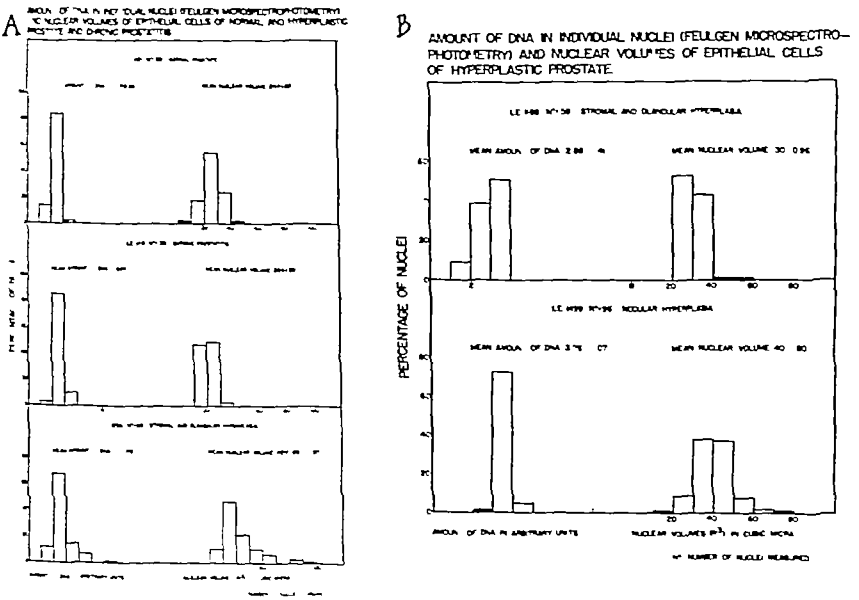


FIG 2

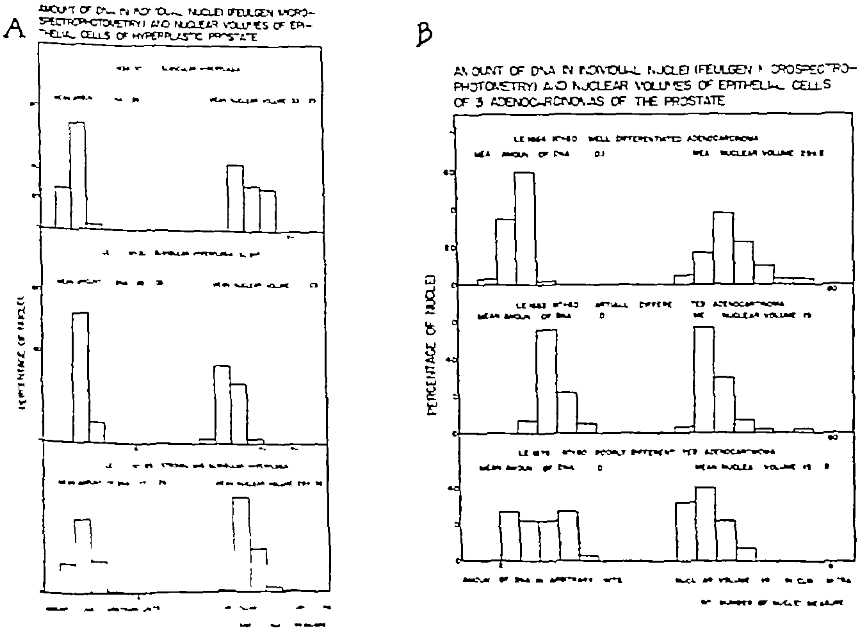


FIG 3

that the nuclear volumes for the benign and malignant cases show a rather wide range of values with a very similar distribution curve

In figures 2–4 the individual DNA and nuclear volumes data of several representative examples of both the benign and malignant cases are presented Upon

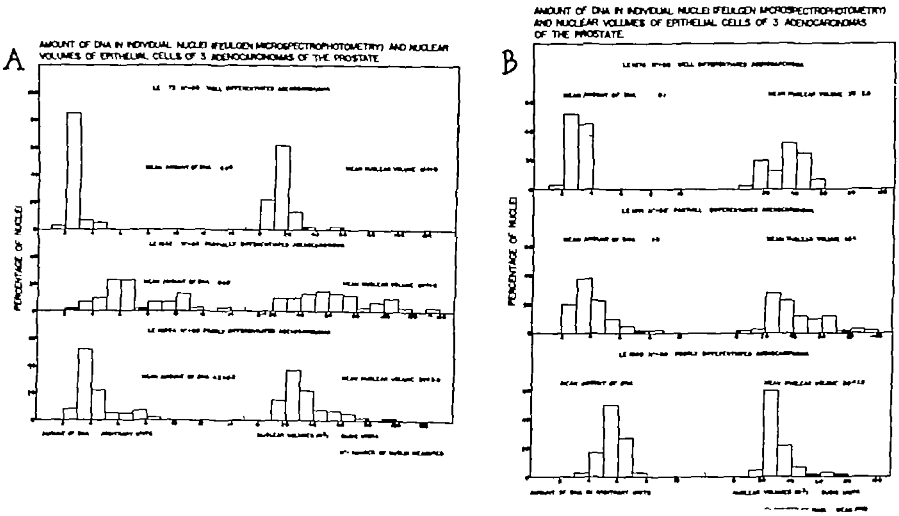


Fig 4

examination, it was found that the DNA values for the individual cells are again constant within the benign group, in contrast to the wide scatter found within the individual cells of the malignant group Consideration of the individual cell volumes corroborates the graphic demonstration (fig 1) of the mean volumes

DISCUSSION

Summarizing briefly, the DNA values in the epithelial cells of the benign hyperplastic and hypertrophic lesions which have been examined correspond to the characteristic and constant values of normal prostates and other normal human tissues The DNA results for these benign lesions are somewhat surprising, especially where the diagnosis of hyperplasia has been made A priori, one would expect that an area of hyperplasia, i e , a tissue which is multiplying and producing new cells, *would show an increase in the DNA values within the cell nuclei* It is well known that in such zones of hyperplasia even normal cells, such as embryonic or regenerating cells, which prepare for mitoses show a gradual doubling of their DNA as compared with the constant DNA content in cells of nondividing tissues Therefore, *an unchanged DNA content in cells of a hyperplastic tumor* is certainly a puzzling finding It is an even greater enigma in view of the fact that *benign tumors from other tissues have always revealed the expected DNA* synthesis

On the other hand, the constant DNA values found in these hyperplastic prostates are in accordance with the cytological observations made in these same specimens In spite of careful cytological examination and extensive search within these hyperplastic glands, mitotic figures were rarely encountered Since there is this lack of mitoses associated with a lack of DNA doubling, characteristic for the formation of new cells, enlargement of the tissue must have occurred either previous to the surgery or be progressing at a very slow rate It is felt that the integration of the cytochemical data with the clinical and histopathological

TABLE 1 *Mean amounts of DNA in nuclei and nuclear volumes of epithelial cells from benign hypertrophic, hyperplastic and malignant prostatic glands*

Case No	Age	Diagnosis	Number of Nuclei Measured	Mean Amount of DNA in Arbitrary Units	Mean Nuclear Volume—r³ in Cubic Micra
1053 B	75	Benign glandular hyperplasia	30	2.36 ± 0.14	33 ± 1.25
1113	80	Chronic prostatitis	30	2.64 ± 0.06	20.0 ± 1.2
1114	67	Glandular hyperplasia, slight	30	2.65 ± 0.05	19 ± 1.03
1115	56	Hypertrophy and hyperplastic enlargement	20	2.65 ± 0.07	19 ± 1.00
1118 A	65	Glandular hyperplasia, slight	34	2.58 ± 0.05	21 ± 1.15
1119	73	Nodular, glandular hyperplasia	25	2.22 ± 0.04	25 ± 1.10
1120	41	Normal	26	2.80 ± 0.06	23 ± 1.58
1121	35	Normal	50	2.38 ± 0.08	24 ± 1.05
1167	56	Stromal and glandular hyperplasia	30	2.30 ± 0.07	57 ± 2.36
1165	66	Stromal and glandular hyperplasia	58	2.86 ± 0.41	30 ± 0.96
1206	60	Stromal and glandular hyperplasia	60	2.80 ± 0.14	40 ± 1.89
1207	60	Stromal and glandular hyperplasia	57	2.55 ± 0.06	34 ± 1.35
1215	59	Stromal and glandular hyperplasia	85	2.77 ± 0.26	28 ± 1.38
1479	29	Hyperplasia	70	1.61 ± 0.08	28 ± 1.7
1499	58	Nodular hyperplasia with focal cystic formation	96	3.26 ± 0.07	40 ± 1.8
1559	71	Poorly differentiated squamous cell carcinoma	100	2.8 ± 0.1	56 ± 3
1644	81	Particles of diffusely growing anaplastic carcinoma	60	3.7 ± 0.1	41 ± 4
1645	60	Metastatic adenocarcinoma of prostate	80	3.8 ± 0.1	37 ± 3
1648	72	Moderately well differentiated adenocarcinoma	60	2.8 ± 0.1	38 ± 2
1652 A	75	Fragments of partially differentiated adenocarcinoma	60	7.0 ± 0.3	67 ± 1
1649	68	Diffusely growing partly tubular small cell carcinoma	60	3.8 ± 0.2	24 ± 1.5
1664	63	Well differentiated adenocarcinoma Glandular hyperplasia Chronic prostatitis Chronic urethritis	60	3.1 ± 0.1	29 ± 2
1657 A	75	Well differentiated adenocarcinoma Glandular and stromal hyperplasia Focal chronic prostatitis	60	3.2 ± 0.1	19 ± 1
[illegible]	84	Well differentiated adenocarcinoma Glandular and stromal hyperplasia Acute and chronic prostatitis	60	2.9 ± 0.1	50 ± 1
1671	61	Partially differentiated adenocarcinoma glandular	60	4.0 ± 0.2	43 ± 5
1672 B	59	Partially differentiated adenocarcinoma	60	3.0 ± 0.1	26 ± 6
1674	57	Partially differentiated adenocarcinoma Chronic prostatitis—focal stromal hyperplasia	60	3.4 ± 0.2	29 ± 2

TABLE 1 *Concluded*

Case No	Age	Diagnosis	Number of Nuclei Measured	Mean Amount of DNA in Arbitrary Units	Mean Nuclear Volume—r³ in Cubic Micra
1675	55	Poorly differentiated adenocarcinoma with invasions of seminal vesicles showing necrosis and extensive *inflammatory reaction*	60	3.4 ± 0.2	36 ± 3
1676	68	Well differentiated adenocarcinoma Glandular hyperplasia Chronic and focal ac prostatitis Prostatic calculi, urinary calculi	60	2.8 ± 0.1	33 ± 5
1673	64	Moderately well differentiated adenocarcinoma	60	2.6 ± 0.1	15 ± 1
1677	71	*Partially differentiated* adenocarcinoma Acute and chronic prostatitis Glandular and stromal hyperplasia	60	2.9 ± 0.1	14 ± 1
1678	85	Poorly differentiated adenocarcinoma Acute and chronic prostatitis and urethritis	60	4.1 ± 0.2	15 ± 1
1679	72	*Poorly differentiated adenocarcinoma*	60	2.8 ± 0.1	11 ± 1
1680	73	Poorly differentiated adenoca Focal sq metaplastia of ure mucosa Chr prostatitis	60	5.5 ± 0.1	30 ± 1.5
1681	78	Poorly differentiated adenocarcinoma	60	3.0 ± 0.2	47 ± 2.5
1682	68	Partially differentiated adenocarcinoma	60	4.2 ± 0.2	37 ± 3
1683	81	Partially differentiated adenocarcinoma	60	4.6 ± 0.1	19 ± 1
1684	71	Atypical papillary hyperplasia, the *possibility of ca is not excluded*	60	3.7 ± 0.1	32 ± 2
1799	72	Well differentiated adenocarcinoma	60	2.8 ± 0.1	12 ± 1
1800	75	Diffuse well differentiated adenocarcinoma	60	6.0 ± 0.2	39 ± 2

findings is helpful in obtaining a better understanding of the true nature of these benign lesions The suggestion that the benign lesions are the remains of a previous stimulus, with little residual growth activity seems justified and is corroborated by their clinical course Further support for this concept is afforded by the data of nuclear size As can be seen in table 1 and figure 1, the nuclear sizes of the epithelium from the benign lesions are significantly larger than those of the normal, an observation which would suggest that the growth of the organ may not solely be caused by an increase in the number of cells, that is, hyperplasia, but it may be partly due to the growth of the individual cells, namely, hypertrophy

In contrast to these unexpected DNA values in the benign enlargements, the DNA values for the malignant lesions are in good accordance with the data for other malignant human tissues These prostatic tumors as do the other human tumors, show not only an increase in the amount of the DNA, but also a relatively wide scatter of the individual DNA values, indicating a buildup of DNA in individual nuclei in preparation for mitoses Moreover, cytological studies in these cases of true prostatic neoplasm revealed frequently, but not always, mitoses the DNA buildup on the other hand was always present As pointed out previously,[6] this synthesis of DNA deserves special consideration, since the absence of mitotic figures in a tissue does not exclude the possibility that a mitotic process is going on If the time period of a mitotic cycle is a very rapid one, mitotic figures may be missed completely Since DNA synthesis occurs at a very early stage of the mitotic process, and is relatively independent of the time period of the mitotic cycle, DNA increase can be used as a most sensitive indicator for cell division

Studies of this kind may be particularly helpful to the urologist and pathologist when a definite diagnosis cannot be reached in the consideration of the suspicious prostatic biopsy When an area of DNA buildup is demonstrated in such a specimen, one would feel more secure in proceeding with radical surgery In the occult carcinoma as well, where the surgeon favors conservative management or decides, because of the over-all clinical picture, not to proceed with total prostatectomy, DNA measurement may be a worthwhile diagnostic tool A failure to demonstrate a buildup of DNA would suggest that in terms of the growth potential, the tumor is of relatively low grade activity, at least at the time of the biopsy This would possibly strengthen the surgeon's resolve to manage conservatively Contrariwise, increase in the DNA would suggest that a bolder attack on the lesion is in order Thus, we feel that our initial study has demonstrated that microspectrophotometric data may be a valuable addition in the clinical evaluation and management of prostatic tumors Possibly its use can be extended into a more accurate appreciation of the changes in prostatic epithelium secondary to orchiectomy and the use of estrogens or corticoids Certainly, it is reasonable to conclude that DNA measurements will contribute to a better over all understanding of prostatic disease processes

SUMMARY

Microspectrophotometric studies of the DNA content in 2,261 cells in 15 benign and normal prostates and 25 carcinomas of the prostate were carried out Results showed that benign enlargements had essentially normal DNA content Malignant cells showed the expected scatter and buildup of DNA values The possibility of using DNA measurements as a diagnostic aid in questionable tumors is discussed

TABLE 1 *Concluded*

Case No	Age	Diagnosis	Number of Nuclei Measured	Mean Amount of DNA in Arbitrary Units	Mean Nuclear Volume—r³ in Cubic Micra
1675	55	Poorly differentiated adenocarcinoma with invasions of seminal vesicles showing necrosis and extensive inflammatory reaction	60	3 4 ± 0 2	36 ± 3
1676	68	Well differentiated adenocarcinoma Glandular hyperplasia Chronic and focal ac prostatitis Prostatic calculi, urinary calculi	60	2 8 ± 0 1	33 ± 5
1673	64	Moderately well differentiated adenocarcinoma	60	2 6 ± 0 1	15 ± 1
1677	71	Partially differentiated adenocarcinoma Acute and chronic prostatitis Glandular and stromal hyperplasia	60	2 9 ± 0 1	14 ± 1
1678	85	Poorly differentiated adenocarcinoma Acute and chronic prostatitis and urethritis	60	4 1 ± 0 2	15 ± 1
1679	72	Poorly differentiated adenocarcinoma	60	2 8 ± 0 1	11 ± 1
1680	73	Poorly differentiated adenoca Focal sq metaplastia of ure mucosa Chr prostatitis	60	5 5 ± 0 1	30 ± 1 5
1681	78	Poorly differentiated adenocarcinoma	60	3 0 ± 0 2	47 ± 2 5
1682	68	Partially differentiated adenocarcinoma	60	4 2 ± 0 2	37 ± 3
1683	81	Partially differentiated adenocarcinoma	60	4 6 ± 0 1	19 ± 1
1684	71	Atypical papillary hyperplasia, the possibility of ca is not excluded	60	3 7 ± 0 1	32 ± 2
1799	72	Well differentiated adenocarcinoma	60	2 8 ± 0 1	12 ± 1
1800	75	Diffuse well differentiated adenocarcinoma	60	6 0 ± 0 2	39 ± 2

findings is helpful in obtaining a better understanding of the true nature of these benign lesions The suggestion that the benign lesions are the remains of a previous stimulus, with little residual growth activity seems justified and is corroborated by their clinical course Further support for this concept is afforded by the data of nuclear size As can be seen in table 1 and figure 1, the nuclear sizes of the epithelium from the benign lesions are significantly larger than those of the normal, an observation which would suggest that the growth of the organ may not solely be caused by an increase in the number of cells, that is, hyperplasia, but it may be partly due to the growth of the individual cells, namely, hypertrophy

In contrast to these unexpected DNA values in the benign enlargements, the DNA values for the malignant lesions are in good accordance with the data for other malignant human tissues These prostatic tumors as do the other human tumors, show not only an increase in the amount of the DNA, but also a relatively wide scatter of the individual DNA values, indicating a buildup of DNA in individual nuclei in preparation for mitoses Moreover, cytological studies in these cases of true prostatic neoplasm revealed frequently, but not always, mitoses, the DNA buildup on the other hand was always present As pointed out previously,[6] this synthesis of DNA deserves special consideration, since the absence of mitotic figures in a tissue does not exclude the possibility that a mitotic process is going on If the time period of a mitotic cycle is a very rapid one, mitotic figures may be missed completely Since DNA synthesis occurs at a very early stage of the mitotic process, and is relatively independent of the time period of the mitotic cycle, DNA increase can be used as a most sensitive indicator for cell division

Studies of this kind may be particularly helpful to the urologist and pathologist when a definite diagnosis cannot be reached in the consideration of the suspicious prostatic biopsy When an area of DNA buildup is demonstrated in such a specimen, one would feel more secure in proceeding with radical surgery In the occult carcinoma as well, where the surgeon favors conservative management or decides, because of the over-all clinical picture, not to proceed with total prostatectomy, DNA measurement may be a worthwhile diagnostic tool A failure to demonstrate a buildup of DNA would suggest that in terms of the growth potential, the tumor is of relatively low grade activity, at least at the time of the biopsy This would possibly strengthen the surgeon's resolve to manage conservatively Contrariwise, increase in the DNA would suggest that a bolder attack on the lesion is in order Thus, we feel that our initial study has demonstrated that microspectrophotometric data may be a valuable addition in the clinical evaluation and management of prostatic tumors Possibly its use can be extended into a more accurate appreciation of the changes in prostatic epithelium secondary to orchiectomy and the use of estrogens or corticoids Certainly, it is reasonable to conclude that DNA measurements will contribute to a better over all understanding of prostatic disease processes

SUMMARY

Microspectrophotometric studies of the DNA content in 2,261 cells in 15 benign and normal prostates and 25 carcinomas of the prostate were carried out Results showed that benign enlargements had essentially normal DNA content Malignant cells showed the expected scatter and buildup of DNA values The possibility of using DNA measurements as a diagnostic aid in questionable tumors is discussed

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THE UROGENITAL SINUS ITS DEMONSTRATION AND SIGNIFICANCE

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A patient whose sex is in doubt confronts the physician as a difficult diagnostic and therapeutic problem The nature of the gonads does not invariably dictate whether such an individual should be reared as a man or as a woman, nor whether the patient should continue in the sexual category of his upbringing Money, Hampson and Hampson[1] have pointed out that in hermaphroditism there are diverse contradictions between seven determinatives of sex 1) chromosomal sex, 2) gonadal sex, 3) hormonal sex, 4) internal accessory reproductive structures, 5) external genital morphology, 6) sex of assignment and rearing, and 7) gender role and orientation established while growing up Each of these variables must be considered before assignment of sex and choice of treatment are made Our study is concerned with the fourth variable, the internal accessory reproductive structures and their relations to the urinary tract Cystoscopic and radiographic visualization of the urogenital structures aid in the assignment of the proper sex and in the selection of surgical procedures which will make the urinary and genital structures compatible with the sex assigned

During the investigation of patients with congenital anomalies of the genitalia, the authors frequently found a urogenital sinus As this structure is normally seen only in the indifferent stage of the embryo, its persistence indicated that the patient's gender was doubtful in some degree In such persons the urogenital sinus arose at the confluence of the urethra and the internal genitalia derived from the müllerian duct The urinary and genital tracts thus shared a common passage to the exterior and a common cutaneous aperture on the perineum The relation between the urogenital sinus and the urinary and genital tracts has been of two general anatomical types In the first, the urogenital sinus and *urethra* appeared to be continuous, the vagina entering at the distinct angle in the floor of this continuous passage (fig 1) This general plan was seen most commonly in male pseudohermaphrodites In the second type the urogenital sinus and *vagina* appeared to be continuous, the urethra opening at an angle in the roof of the common passage (fig 2) This second type was seen most commonly in female pseudohermaphrodites At times the urethral opening was found just within the cutaneous aperture of the urogenital sinus, but at other times it was found several centimeters from the cutaneous surface (fig 3) In one patient the urethra joined the urogenital sinus approximately two centimeters from the perineal aperture but an additional patent urethra was found traversing the phallus from a point in

Accepted for publication June 25 1957

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[1] Money, J , Hampson, J G and Hampson, J L An examination of some basic sexual concepts Evidence of human hermaphroditism Bull Johns Hopkins Hosp , 97 301–319, 1955

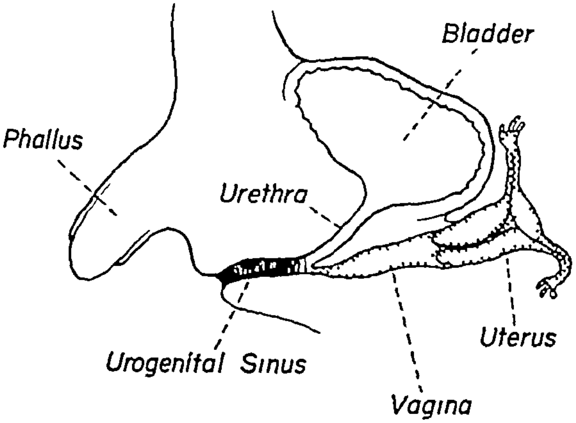

FIG 1 In male pseudohermaphrodites, urogenital sinus and *urethra* frequently appear to be continuous Opening to vagina is in floor of this continuous passage and makes its entrance at a distinct angle

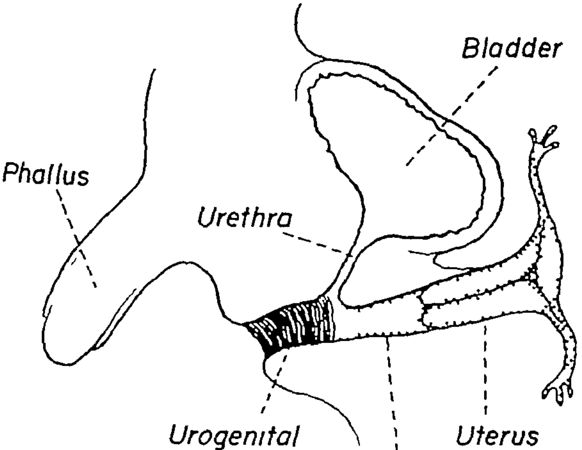

FIG 2 In female pseudohermaphrodites, urogenital sinus and *vagina* frequently appear to be continuous Urethra opens at an angle into anterior aspect of passage

the anterior aspect of the urogenital sinus about one to two millimeters distal to the junction of the proximal urethra with the vagina (fig 7)

Our usual diagnostic plan has been to visualize the internal structures by cystoendoscopy and then to record permanently their relationships by radiographic techniques An oblique projection of the pelvis after the selective instillation of contrast medium through catheters separately inserted into the bladder and vagina allowed best visualization of the relationship of the internal accessory reproductive structures to the urinary tract Air and one of the water soluble organic iodides have been employed as contrast media When a cervix has been present, a ureteral catheter could be passed gently into the os and a hysterogram

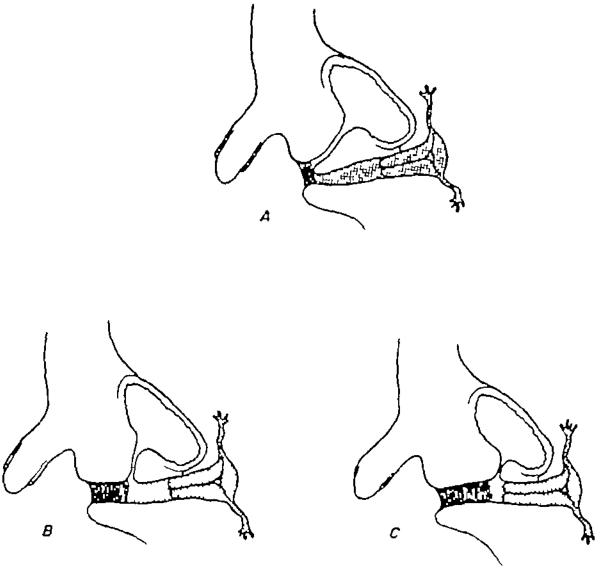

FIG 3 In female pseudohermaphrodites, urethra usually joins continuous passage *formed by urogenital sinus and vagina in midline anteriorly, but at no specified point* Urogenital sinus might be quite short, as in *A*, quite long as in *C*, or of any length between these two extremes, as exemplified by *B*

obtained Finally, after the catheters were removed, a film was exposed during the steady injection of a more concentrated contrast medium from a syringe fitted in the external opening of the urogenital sinus

A urogenital sinus has been observed in female pseudohermaphrodites with adrenocortical hyperplasia, female pseudohermaphrodites without evidence of adrenocortical hyperplasia, a true hermaphrodite, and male pseudohermaphrodites

FEMALE PSEUDOHERMAPHRODITISM WITH ADRENOCORTICAL HYPERPLASIA

Virilizing adrenocortical hyperplasia is a well known adrenogenital syndrome[2] When the condition exists prenatally, the female pseudohermaphrodite is born with various abnormalities of the external genitalia and shows hypertrophy of the clitoris and a single opening at the base of the phallus which is the opening of the urogenital sinus Such a female patient is often mistaken for a boy Rarely there may be a urethra through the phallus The persistence of the urogenital sinus is due to the adrenal overstimulation which occurs after the twelfth week of gestation, when the genital duct differentiation is complete, but before the twentieth week, *when the normal relationship of the urethra and vagina is established* (fig 4) If continued overproduction of the androgenic substances by the adrenal cortex occurs postnatally there is accelerated muscular and osseous development and progressive virilization Many of these patients develop adrenal insufficiency The diagnosis is established by demonstrating elevated levels of 17-ketosteroids

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[2] Wilkins, L Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence Springfield, Ill Charles C Thomas, 1950

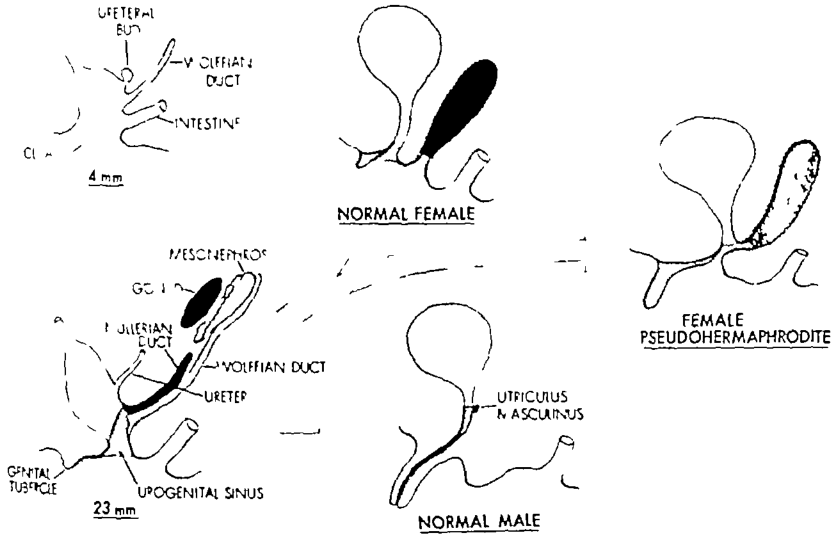

FIG 4 Schematic illustration (after Wilkins) of development of normal female anatomy, normal male anatomy and structures in female pseudohermaphrodite from embryonic structures

and pregnanetriol in the urine of a patient with a hypertrophied phallus and a urogenital sinus If the patient is beyond early infancy evidence of excessive virilization will be present Radiographic study will usually demonstrate a urogenital sinus and developed mullerian components This disorder responds well to low maintenance doses of cortisone with resultant normal female growth and development The following are selected from our group of 19 cases of adrenogenital syndrome

Case 1 (AK, NYH No 670904) A three-month-old child at birth was thought to be a boy with hypospadias, bifid scrotum and undescended testicles, fed poorly and gradually became marasmic and dehydrated The infant was treated with intravenous fluids, blood, DOCA and added salt in the diet The pendulous portion of the hypospadiac phallus was 3 cm in length The scrotum was bifid and empty The urethral opening was in the perineum The urinary excretion of 17-ketosteroids was 6 57 mg per 24 hours The serum potassium was 6 5 meq/L, while the serum chloride and sodium concentrations were 88 8 meq/L and 125 meq/L respectively A cystourethrogram (fig 5) demonstrated a vagina which joined the urethra to form a urogenital sinus (our type 1) Endoscopically the small opening of the vagina was located in the floor of the urogenital sinus just proximal to the external sphincter The bladder appeared normal The patient improved with administration of cortisone and sodium chloride Skin and gonadal biopsies were not done but the diagnosis of congenital adrenocortical hyperplasia seemed established The clitoris was excised at the age of 20 months and a

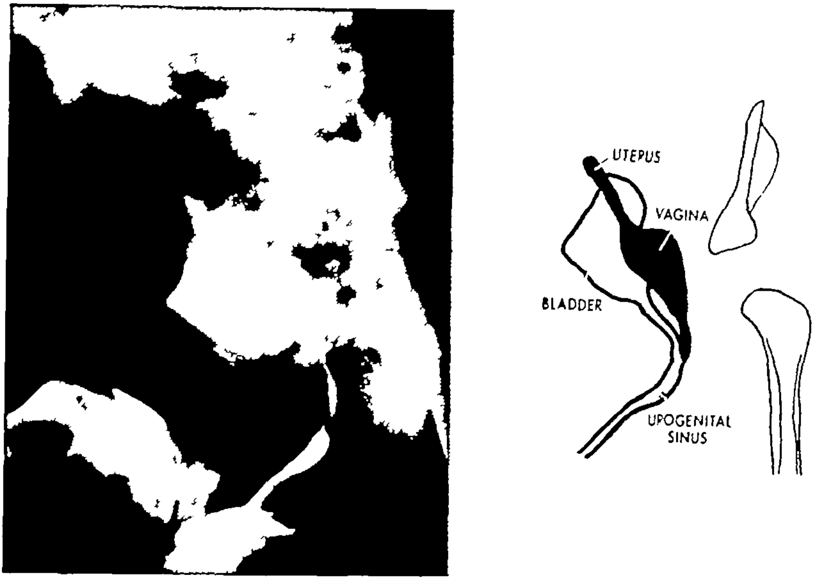

Fig 5 Cystourethrogram and phantom of female pseudohermaphrodite

perineorrhaphy with reconstruction of the labia minora was performed one month later

Case 2 (MW, NYH No 686966) *A* 13-day-old baby had been vomiting persistently for five days and was admitted in respiratory distress with a pulse of 200 per minute An enlarged clitoris had been noted at birth Urine passed from a meatus, anteriorly located at the perineum The labia were large but empty The serum potassium was 10 4 meq/L, chlorides, 85 7 meq/L, and sodium, 120 meq/L An electrocardiogram showed depressed S-T segments, absence of P waves, and extraventricular beats Management of fluid and electrolytes and the administration of DOCA and compound F brought prompt improvement Later the urinary excretion of 17-ketosteroids was 8 1 mg per 24 hours The bone age was advanced Radiographic studies demonstrated a vaginal pouch joining the urethra and a uterine canal joining the vagina (fig 6) Skin and gonadal biopsies were not done A partial clitorectomy and plastic perineotomy produced a female perineum The diagnosis was aided by the fact that one sibling was known to have congenital adrenocortical hyperplasia The patient, now two and a half years of age, has remained well on maintenance cortisone therapy

FEMALE PSEUDOHERMAPHRODITISM WITHOUT ADRENOCORTICAL HYPERPLASIA

Female pseudohermaphrodites without evidence of adrenocortical hyperplasia are born with evidence of prenatal adrenal overstimulation manifested by a hypertrophied phallus and a urogenital sinus There is no evidence of excessive somatic growth, their urinary 17-ketosteroids and pregnanetriol levels are normal Such patients have been mistakenly reared as cryptorchid boys with hypospadias At puberty they acquire female secondary sexual characteristics Cystourethrographic study will demonstrate the urogenital sinus and mullerian derivatives The following example has been selected from our two cases

Case 3 (BB, NYH No 698124) A three-and-a-half-year-old child was admitted because of an enlarged clitoris which had been noted since birth The physical examination was normal except for an enlarged clitoris, approximately 3 cm long, with a prepuce The labia majora were atrophic and no labia minora were noted A single anterior perineal orifice was present Laboratory studies showed the 24-hour urinary excretion of 17-ketosteroids and the serum electrolyte con-

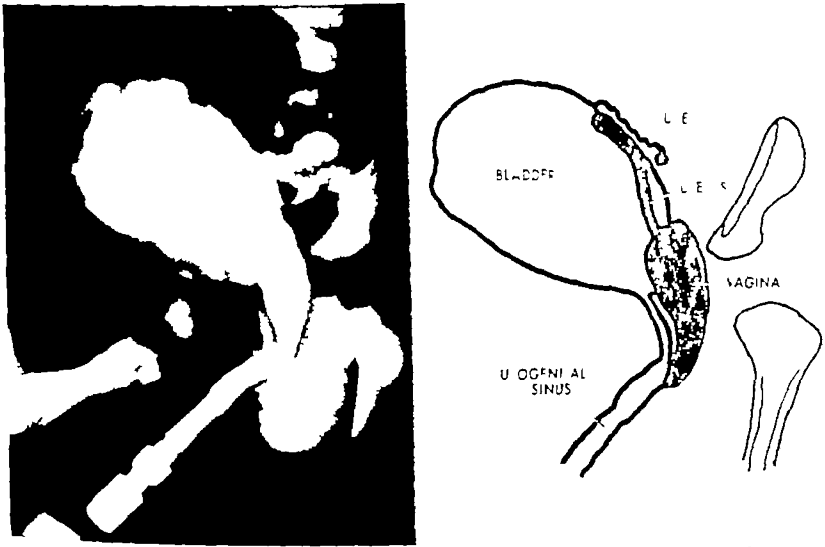

FIG 6 Cystourethrogram and phantom of female pseudohermaphrodite

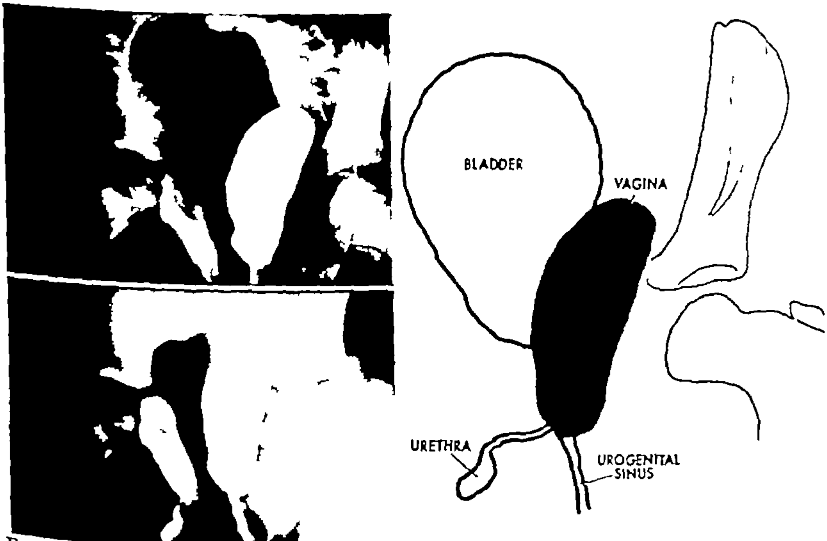

FIG 7 Cystourethrogram and phantom of female pseudohermaphrodite Urethra joins urogenital sinus about 2 cm from perineal aperture but an additional patent urethra traverses phallus

centrations to be normal Cystourethrography (fig 7) and cystourethroscopy disclosed that the patient had two urethras One opened into the urogenital sinus (our type 2) and the other traversed the entire length of the phallus The skeletal age was normal for the patient's age and sex A skin biopsy showed a female chromosomal pattern An exploratory laparotomy revealed normal female internal genitalia and no evidence of testicular tissue Biopsy of both gonads revealed normal ovarian tissue The clitoris was then totally excised She is now five and a half years of age and is symptom-free

MALE PSEUDOHERMAPHRODITISM

Male pseudohermaphrodites may present a fully formed penis with penile urethra, but the greater number present as cryptorchid hypospadiac males Money and associates[1] place the cryptorchid hypospadiac male in a separate category, pointing out that "historically, hypospadiacs have not been called hermaphrodites unless hypospadias is extreme, the scrotum bifid, and the testes undescended " In practice, the radiographic demonstration of the müllerian duct derivative is essential for the diagnosis of male pseudohermaphrodism However, it is our opinion that hypospadiacs represent, in fact, a form of male pseudohermaphrodism In hypospadias, as Howard has pointed out,[3] the more proximal the urethral meatus, the more bifid the scrotum, and the higher the testes, the greater will be the size of the internal genitalia derived from the müllerian duct

Labioscrotal fusion may be so complete that a quite smooth perineum exists or so incomplete as to present a bifid scrotum, a normal vulva, or even a large cloacal defect Male pseudohermaphrodites have no increase in androgenic hormone excretion and secondary sexual characteristics do not develop until puberty Rarely, there may be separate vaginal and urethral openings The testis may be in the labial fold, groin, or abdomen The following are three examples of male pseudohermaphrodism

Case 4 (AE, NYH No 412817) A nine-year-old child, admitted on September 12, 1954, had been known from birth to have chordee, perineal hypospadias, a bifid scrotum, and bilateral cryptorchism Physical examination was otherwise normal Laboratory examinations, including serum electrolyte concentrations and the urinary excretion of 17-ketosteroids, were within normal limits Cystourethrography and cystourethroscopy (fig 8) revealed a communication between the urethra and the vagina The contrast material extended from the vagina into the uterus and fallopian tubes Pyelograms showed partial obstruction of the left ureterovesical junction with mild hydronephrosis of the left kidney The right kidney was of normal appearance The skeletal age was normal A psychiatric consultant reported the patient to be psychologically masculine An exploratory celiotomy demonstrated a vagina, uterus and tubes, but no evidence of ovarian tissue The intrapelvic gonads proved to be testes when biopsied The remnant of the intrapelvic right testicle was removed The left testicle, found on the left lateral pelvic wall, was brought down into the scrotum The proximal end of the vagina, uterus and tubes were excised and a left ureteroneocystostomy was performed

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[3] Howard, F S The surgery of intersexuals J Urol , 65 636–649, 1951

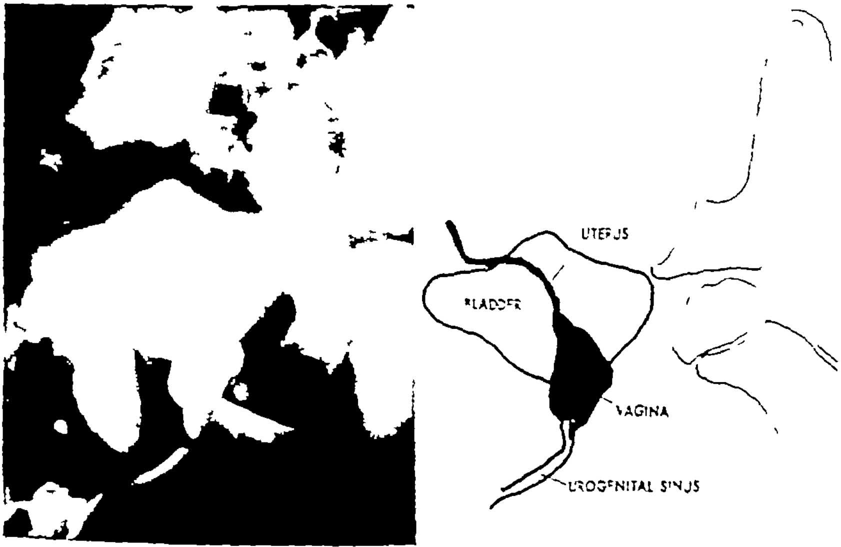

FIG 8 Cystourethrogram and phantom of male pseudohermaphrodite

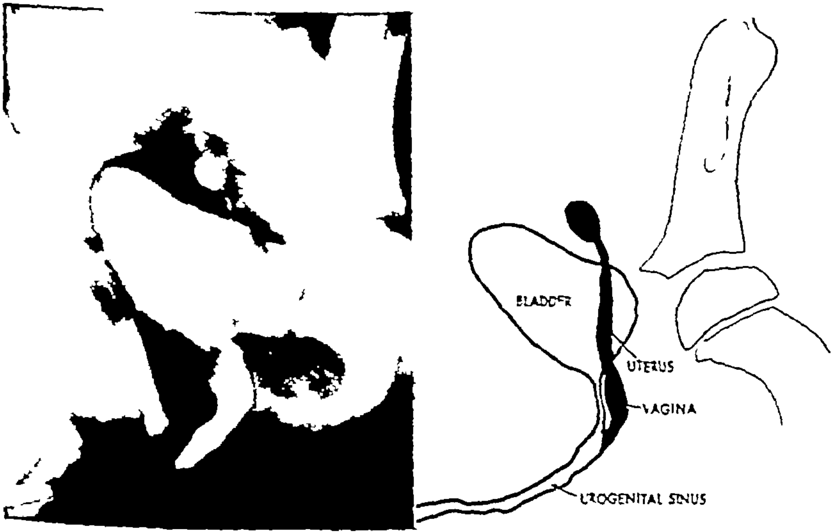

FIG 9 Cystourethrogram and phantom of male pseudohermaphrodite

Microscopic examination of the excised tissues identified vagina, fallopian tubes, vas deferens, and testes A biopsy of skin revealed a male chromosomal pattern Correction of the chordee was performed on October 19, 1954 and construction of the urethra with bladder mucosal graft was performed nine months later[4] In September 1956 the patient was well except for a persistent small perineal sinus

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[4] Marshall, V F and Spellman R M Construction of urethra in hypospadias using vesical mucosal grafts J Urol 73 335–342 1955

Case 5 (WB, NYH No 462847) Examination of a three-year-old Negro child revealed penoscrotal hypospadias with chordee, a bifid scrotum and bilaterally undescended testes The kidneys and ureters appeared normal by intravenous pyelography Routine laboratory studies were within normal limits A cystourethrogram (fig 9) showed a small vagina joining the urethra to form a urogenital sinus Exploration of the pelvis disclosed a vagina, uterus and tubes, at the end of which were two intrapelvic gonads which on biopsy proved to be testes Skin biopsy was not done The testes reached only to the suprapubic subcutaneous tissue, where they were attached The mullerian remnants were not excised A urethra was constructed, using bladder mucosa [4] The patient has had recurrent urethral strictures but has been otherwise well

Case 6 (RZ, NYH No 576878) A three-and-a-half-year-old patient was found to have a chordee, perineal hypospadias, bifid scrotum, and bilateral undescended testes Growth and development had otherwise been normal The 24-hour urinary excretion of 17-ketosteroids was 0 38 mg The upper urinary tracts appeared normal by intravenous pyelography Cystourethrography and cystourethroscopy revealed a small vagina joining the urethra to form a urogenital sinus (our type 2) (fig 10) The skeletal age was normal The chordee was repaired and the left gonad biopsied and placed in the scrotum The biopsy contained only normal testicular tissue At four years of age a urethra was constructed, using bladder mucosa [4] A skin biopsy was not obtained The patient has been well except for occasional hematuria and some enlargement of his prostate He is now eight years of age

TRUE HERMAPHRODISM

True hermaphrodites have ovarian and testicular tissue, in the form of ovaries, testes, or ovotestes They may present all degrees and variations of external

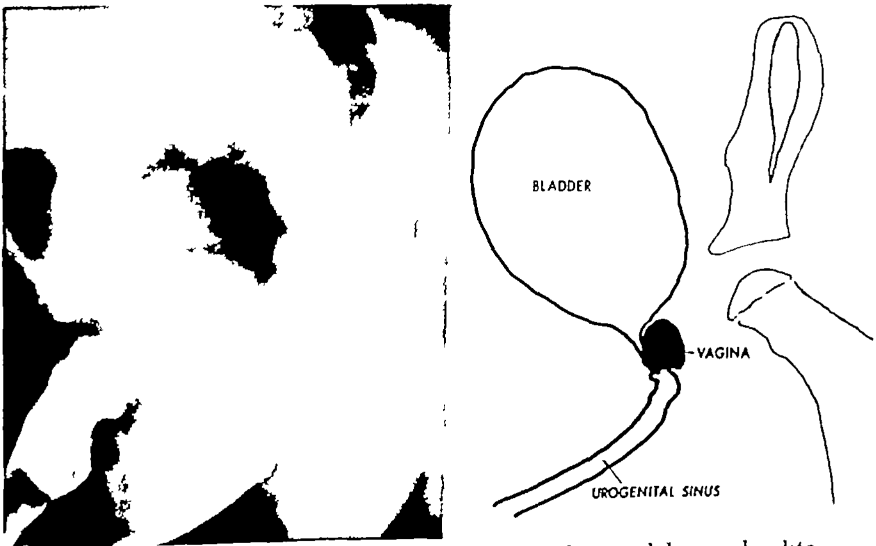

Fig 10 Cystourethrogram and phantom of male pseudohermaphrodite

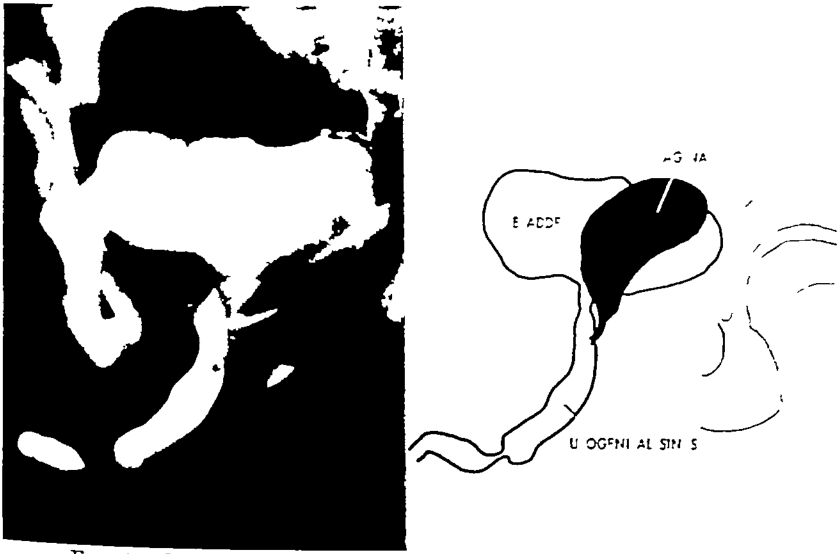

FIG 11 Cystourethrogram and phantom of true hermaphrodite

genital abnormality There may be separate vaginal and urethral openings, but more commonly there is a single opening of the urogenital sinus The phallus, according to Gross,[5] is usually larger than a clitoris but smaller than a normal penis, and is hypospadiac

In this group of patients it is impossible to predict which hormonal pattern will predominate at puberty Therefore, the correct assignment of sex is especially difficult Cystourethrographic studies reveal the status of müllerian derivatives and thus aid in the over-all evaluation of these very difficult problems Diagnosis requires exploratory laparotomy and biopsy of the gonads, as well as psychological evaluation.

The following case, which has been previously reported,[6] has been selected from our two cases of true hermaphrodism

Case 7 (PD, NYH No 161423) A 15-year-old patient had had a repair of a chordee, construction of a urethra from the perineal meatus to the glans, using skin, and a left orchiopexy seven years before He had noted enlargement of both breasts at 14 years of age On examination, a palpable, nontender mass was found in the left inguinal region extending toward the left side of the scrotum The right side of the scrotum contained a mass 2 cm in diameter with a hard nodule 3 mm in diameter at the lower pole The breasts were enlarged and contained firm mammary tissue The pendulous portion of the urethra was 6 cm in length and of proportionate caliber Laboratory tests, including Aschheim-Zondek test, 17-ketosteroid excretion studies and serum electrolyte concentrations, were normal Endoscopy disclosed a 3 mm. aperture on the floor of the urethra just proximal to the verumontanum which proved to be the opening of a vagina This

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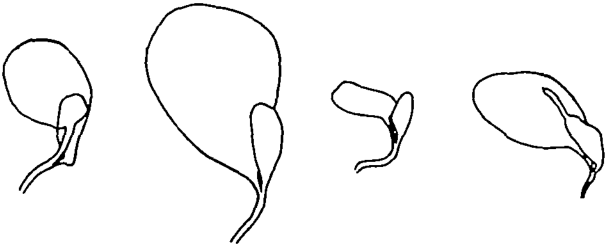
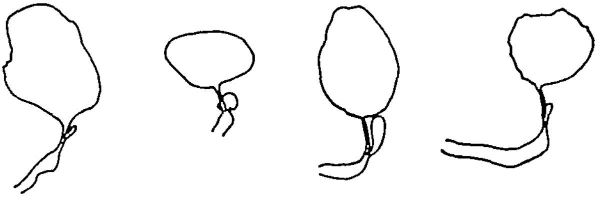
[5] Gross, P W and Meeker I A Jr Abnormalities of sexual development Observations from 75 cases Pediatrics 16 303-324 1955

[6] Marshall V F Paquin A J Jr and Pearce J M True hermaphroditism Conference on management of one patient J Urol 72 77-86, 1954



FEMALE PSEUDOHERMAPHRODITE



MALE PSEUDOHERMAPHRODITE

Fig 12 Composite drawing illustrates some variations found in cystourethrograms of female and male pseudohermaphrodites

latter structure had transverse rugae and a small cervix at its proximal end A large vagina joining the urethra to form a urogenital sinus was seen on cystourethrography (fig 11) A hysterogram demonstrated a rudimentary uterine cavity which inclined toward the left The mass excised from the left groin was found to be ovarian tissue on microscopic examination Biopsy of the right scrotal mass disclosed an ovotestis A skin biopsy was not done A psychiatric consultant stated that the patient clearly was psychologically masculine He had been reared as a boy At a subsequent operation no intraperitoneal gonadal tissue was found During the procedure the tapering uterus was totally removed, the upper end of the vagina closed, and the hypertrophied mammary tissue excised

DISCUSSION

Figure 12 is a composite of the various types of urogenital sinuses we have encountered The urogenital sinus has been seen in all the forms of hermaphrodism listed earlier The appearances of the genitourinary tract outlined with contrast medium in the various types of hermaphrodism are radiographically similar[7] True hermaphrodites, male pseudohermaphrodites and female pseudohermaphrodites may all show the same clearly defined urogenital sinus distal to the junction of mullerian derivatives and urethra Failure to demonstrate a urogenital sinus does not exclude the possibility of hermaphrodism or its variants The vagina may be absent or may not communicate with the urethra[7] The actual demonstration of

Tristan T A , Eberlein, W R and Hope, J W Roentgenologic investigations of patients with heterosexual development Am J Roentgen , 76 562-568, 1956 the urogenital sinus, however, is important for an understanding of the internal anatomy, for confirmation of the general diagnosis of sexual ambiguity, and is an aid in the intelligent approach to surgical therapy

SUMMARY

The urogenital sinus is seen in all forms of hermaphrodism but its presence of appearance is not diagnostic of the type of hermaphrodism Cystoscopic and cystourethrographic appearance of the urogenital sinus is exemplified in two female pseudohermaphrodites with adrenocortical hyperplasia and one without evidence of adrenocortical hyperplasia, three male pseudohermaphrodites and one true hermaphrodite

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THE STEROIDS

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Basic individual cell metabolism as related to homeostasis is the field in which extended knowledge leads the way to progress in medicine The relation of the steroids to this field is a complex one, far beyond the ability of the human mind to comprehend, insofar as the infinite variable potentialities are concerned The innumerable contributions in the medical research field involving the steroids have provided as spectacular and varied clinical application as any group of chemical substances we utilize in practice It must be emphasized that the enzymes, phospholipids, amino acids and vitamins are intimately related groups of chemicals, which in themselves are fantastically complex I am bringing the steroids to your attention because they are related to data used in treating mental depression, sex organ tissue problems, menstrual imbalance, fertility, potency, shock, hepatic metabolic abnormalities, urinary calculus problems, psychochemical medical problems, anabolic and catabolic cell metabolism, reversibility and irreversibility of inflammatory changes in tissues, general resistance, malignancy, the mechanism of inflammation, stress and geriatrics The steroids have been proven to be elaborated from acetates and/or[1] cholesterol by enzyme action in the testicles, adrenals, ovaries, and peripheral tissues[2] In passing, it is interesting to know that the pharmaceutical chemical houses utilize enzyme action to produce the various steroids, and that enzyme systems are used in clinical research laboratories in quantitative and qualitative analytical techniques The liver may be involved to a greater degree than any other organ insofar as the individual's steroid pattern is concerned Today there are sixty or more identified steroid compounds Our steroid pattern analytical facilities at this time do not usually include more than five, and these patterns are not reliable as regards quantitative and qualitative results obtained

One most important fact is that any steroid introduced into any human chemical economy may be metabolized or changed to innumerable other steroids in varying percentages and proportions An androgen, for instance, may be administered to a woman and the urinary pattern show an increase in estrogen and little or no increase in the androgen and vice versa

In view of the fact that the antiphlogistic steroids save lives from rapidly progressive and overwhelming infectious inflammatory clinical entities, certain phases of the mechanism of inflammation will be presented The antiphlogistic steroids and ACTH retard inflammation through their inhibitory effect on cellular enzyme metabolism[3] They also interfere with the elaboration of histamine

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Read at annual meeting of American Urological Association, Pittsburgh, Pa , May 6-9, 1957

[1] Block Konrad and Rittenberg, D An estimation of acetic acid formation in the rat J Biol Chem 159 45-58, 1945

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in the mechanism of inflammation[3] The relationship of dosage of these chemicals to clinical situations is so misunderstood that lives are lost because they are not given and because the dosage employed is inappropriate The untoward effects feared are intestinal necrosis and perforation, electrolytic imbalance poor healing and inhibition of antibody formation When the steroids are given, deficiency replacement is one thing and overloading is another Without extending this phase of our discussion further, it has been observed and my experience has demonstrated that 10 to 50 mg of cortisone or hydrocortisone may be administered without much chance of any of the untoward reactions above mentioned occurring In the event any should occur, they should be accepted as a calculated risk The 10 and 25 mg dose of these steroids has proven spectacularly effective in my hands[4]

The antiphlogistic steroids are employed by some anesthetists during surgery and in the recovery room when it appears stress is pronounced[5]

When cortisone, in amounts of 150 to 300 mg daily dosage, is employed in the management of adrenalectomy, healing has not been a problem

To compensate for the antibody deficiency, the antibiotic and chemotherapeutic bactericidal substances should be used in large doses during the administration of the antiphlogistic steroids and continued for appropriate periods after the steroids have been discontinued[6]

In my hands, as small a dose as 1 mg hydrocortisone has proved effective in reducing or preventing frequently recurring pyuria when given over a period of months[7]

Psychochemistry is a profound field The British have demonstrated that mental patients who are impotent and carrying a practically zero ketosteroid level become potent and the ketosteroids return to normal levels after prefrontal lobotomy Dr George Thorn[8] has observed the effect of stress, physical and mental, on Harvard rowing crews, coxswains and coaches with the result that under the stress of the Yale-Harvard race, the stress phenomenon of all was approximately the same, whereas under practice conditions, neither the coach nor the coxswain experienced anywhere near the degree of eosinophil or trypsin reaction that the crewmen did

He also observed that two of four patients with approximately the same degree of acute arthritis, treated with placebos, improved as spectacularly as the other two who were treated with cortisone and ACTH

The relationship of mental stress to marked phosphaturia, oxalate stone formation and fertility is mentioned in passing

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From a practical viewpoint, it would seem that one of our greatest difficulties in appraising the result of various types of therapy is our inability to separate the effect of the psychochemical effect of our individual personality from that of the therapeutic agent employed

Grading the relative potency of psychochemical influences I would put faith in God as number one, faith in the physician number two, and environmental factors number three, with an occasional reversible potentiality between two and three

The administration of androgen in metastatic breast malignancy and estrogens for metastatic prostatic malignancy, which I referred to in 1941, is only mentioned in passing

The administration of testosterone to mentally deteriorated patients due to senile vascular degeneration is frequently spectacularly effective in producing improvement Twenty-five milligrams of testosterone by hypodermic, two to three times a week, is a reasonable regimen Up to now, no evidence is available to prove that testosterone is carcinogenic This is in marked contrast to estrogens

The dosage of testosterone, in low sperm count patients, is interesting, in that small doses stimulate, and large doses inhibit spermatogenesis, although a marked rebound effect follows the administration of large doses in some instances

The extension of life expectancy from a geriatric standpoint may be related to the steroid pattern A fruitful field of research might be the establishment of the average steroid pattern of the third decade with an evolved method of maintaining this pattern

Space will not permit of further discussion

In conclusion, the steroids have proven spectacularly effective therapeutic agents in many fields of chemotherapy

The appropriate dosage and indications are not widely understood

A surgical patient or a general stress patient whose course is satisfactory should not receive steroid therapy

The patient who appears to be rapidly dying from any aspect of stress should receive the antiphlogistic steroids in appropriate dosage

The interrelationship of the steroids, enzymes, phospholipids, vitamins and amino acids is infinitely complex, but constitutes the field in which advances in medicine have been and are going to be made

Since this paper was read, we have observed one patient on 1 mg hydrocortisone daily in whom ulcer-like symptoms developed

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URINARY STEROID EXCRETION AFTER TOTAL ADRENALECTOMY II LEVELS OF 17-KETOSTEROIDS AND FORMALDEHYDOGENIC SUBSTANCES IN PATIENTS ON VARYING DOSAGES OF CORTISONE ACETATE AND GLYCYRRHIZIN

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It has been suggested[1] that the adrenalectomized patient maintained on glycyrrhizin presents a unique opportunity to study steroid metabolism In the process of undertaking such a study, we have employed the Zimmermann and formaldehydogenic determinations for the quantitative measurement of steroids in urinary extracts Data have been collected on the Zimmermann reaction for 17 ketosteroids both on the crude neutral fraction and on the ketonic fraction after separation with Girard's reagent T Formaldehydogenic determinations have been made on the crude neutral fraction and after its purification by chromatography on silica gel

These data show that ammonium glycyrrhizinate administration has no effect on 17-ketosteroid excretion and that the administration of ammonium glycyrrhizinate results in the appearance in the urine of formaldehydogenic substances which are not corticosteroids

EXPERIMENTAL

One male (A) with metastatic prostatic carcinoma and another (B) with incurable testicular carcinoma were utilized for this study The first was completely castrated, while only one testis was removed from the second patient Total adrenalectomy was finally performed in both patients

Throughout this study, all of the urine was collected as 24-hour samples and immediately refrigerated

For the extraction of 17-ketosteroids, the urine was subjected to hot acid (H_2SO_4) hydrolysis and continuous ether extraction in Kutscher-Steudel extractors for 24 hours[2] The neutral fractions were prepared from the ether extracts by procedures previously described[2] After removal of aliquots for the estimation of total 17-ketosteroids, the neutral fraction was separated into the ketonic and non-ketonic fractions by Girard's reagent T as described by Dobriner and others[2] The Girard separation was repeated on each fraction The 17 ketosteroid content of the neutral and ketonic fractions was measured by the

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Zimmermann reaction using essentially the aqueous alcohol method of Holtorff and Koch [3]

For the hydrolysis, extraction and separation of corticosteroid metabolites in human urine, the methods of Romanoff, and others[4] were utilized The pH of the urine was adjusted to 4 8 with 5 N acetic acid One modification was made in the beta glucuronidase hydrolysis procedure The amount of beta glucuronidase* was increased from 150,000 to 300,000 units per 24 hour sample and the incubation period extended from 24 to 48 hours After adjustment to pH 1 0 with 12 N H_2SO_4, the urine was extracted with redistilled methylene chloride for 24 hours in a Hershberg-Wolfe† continuous extractor The methylene chloride solutions were washed five times with 50 ml of cold 0 1 N NaOH and five times with distilled water The washes were re-extracted with methylene chloride After drying over anhydrous sodium sulfate, the solutions were evaporated to dryness in a water bath at 40° C in a fine stream of nitrogen or in vacuo

Aliquots were removed for formaldehydogenic steroid determinations,[5] and each 24-hour extract was fractionated on silica gel into the most polar (A), the more polar (B) and the less polar (C) fractions by the method described by Romanoff and others [4] A fourth fraction, here called D, consists of the first benzene and benzene ether (2 1) eluates from the silica gel At this point, a number of extracts representing several days' collection (to be specified later) were pooled accordingly into respective fractions A, B, C and D Aliquots were then removed from each one of these fractions for formaldehydogenic steroid determinations [5]

RESULTS

In table 1 are presented data on the 17-ketosteroid content of both the neutral and ketonic fractions from the urine of two patients Patient A had a metastatic carcinoma of the prostate and orchiectomy was performed It can be seen that the 17-ketosteroid titres of the neutral fractions are two to three times greater than those of the ketonic fractions The neutral fraction consistently produced an atypical brownish color with metadinitrobenzene, while the color of the ketonic fraction approached more closely the true "Zimmermann" color as measured by a higher absorption at 510 mu than at 420 mu For example, the neutral fraction of patient A shows a pre-adrenalectomy level of 19 4 ± 1 4 mg , while the level drops to 15 0 ± 1 0 mg after the first adrenal (right) was removed This drop is statistically significant, however, the ketonic fraction obtained after Girard separation showed no such drop in the 17-ketosteroid level after the first adrenal was removed The drop observed in the neutral fraction may be due to a decrease in chromogenic material other than 17-ketosteroid After the second adrenal was removed, however, and the patient was maintained

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* Obtained from Warner-Chilcott Division of Warner Hudnut, Inc , New York, N Y

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TABLE 1 *17 Ketosteroid levels in adrenalectomized patients*

Pt Condition	Daily Treatment	Days	17 Ketosteroids (mg/24 hrs)	
			Neutral Fraction	Ketonic Fraction
A Metastatic carcinoma prostate, orchiectomized	None	9	19.4 ± 1.4*	6.4 ± 0.2
Pre adrenalectomy				
Right adrenal removed	75 mg ACTH (IV) on day of operation	18	15.0 ± 1.0	6.5 ± 0.1
Left adrenal removed	100 mg cortisone acetate (oral)	9	7.9 ± 1.1	3.0 ± 0.1
	50 mg cortisone acetate (oral)	50	8.9 ± 0.7	4.5 ± 0.1
B Carcinoma of testis, adrenalectomized	100 mg cortisone acetate	12	12.3 ± 1.9	
	75 mg cortisone acetate	4	12.9 ± 2.0	
	25 mg cortisone acetate	9	7.6 ± 1.8	
	50 mg cortisone acetate	13	8.3 ± 0.9	4.4 ± 0.2
	50 mg cortisone acetate + 4 gm MAG†	7	9.1 ± 0.2	4.3 ± 0.3
	25 mg cortisone acetate + 4 gm MAG	5	10.1 ± 0.8	2.8 ± 0.2
	10 mg cortisone acetate + 4 gm MAG	20	7.6 ± 0.3	2.9 ± 0.3
	5 mg cortisone acetate + 4 gm MAG	29	6.1 ± 0.3	3.9 ± 0.3

* Means ± standard error, where S.E. = $\sqrt{\frac{\sum d^2}{n(n-1)}}$ where d is the deviation from the mean and n is the number of determinations.

† Mono ammonium glycyrrhizinate.

on cortisone acetate, the 17-ketosteroid level dropped to approximately half of the pre-adrenalectomy level in both the neutral and ketonic fractions.

Patient B was an adrenalectomized patient with one remaining intact testis. An attempt was made to correlate the daily excretion of 17-ketosteroids with the oral daily dose of cortisone acetate administered. Here again it can be seen that the 17 ketosteroid titres of the neutral fractions are roughly 2 to 3 times greater than those of the ketonic fractions. No correlation could possibly be made between the oral cortisone acetate administered and the 17-ketosteroids excreted. There was no change in the urinary 17-ketosteroid content of the ketonic fraction in patient B when to the 50 mg. of cortisone acetate daily 4 gm. of monoammonium glycyrrhizinate (MAG) daily was added. The administration of

MAG does not then produce an alteration in the urinary 17-ketosteroids as determined by the Zimmermann reaction

In table 2 are data on the formaldehydogenic urinary steroid (FS) excretion of patient B This patient was maintained on varying doses of cortisone acetate plus 3 gm of MAG daily FS determinations were made on the total neutral fraction and on the most polar (A), more polar (B), less polar (C), and least

TABLE 2 *Formaldehydogenic substances (FS) in the urine of an adrenalectomized subject*

Period	Treatment	No Days	Total FS mg/24 hrs	FS—mg/24 hour				% Recovery
				Most Polar Fraction A	More Polar Fraction B	Less Polar Fraction C	Least Polar Fraction D	
1	25 mg cortisone acetate + 3 gm MAG*/24 hrs	4	15 62	0 90	6 29	7 16	1 41	97 9
2	50 mg cortisone acetate + 3 gm MAG/24 hrs	7	18 98	1 03	7 05	lost	3 42	—
3	25 mg cortisone acetate + 3 gm MAG/24 hrs	6	27 07	2 31	10 32	16 88	3 10	120 3
4	15 mg cortisone acetate + 3 gm MAG/24 hrs	6	32 06	7 80	11 80	22 02	1 03	114 1
5	5 mg cortisone acetate + 3 gm MAG/24 hrs	8	16 92	2 07	7 90	8 46	0 87	114 1
6	2 5 mg cortisone + 3 gm MAG/24 hrs	2	13 83	1 75	7 79	6 73	1 96	132 0
7	6 + 200 mg dehydroepiandrosterone acetate†	4	13 40	3 00	7 05	4 91	0 38	114 2
8	6 + 200 mg Δ^5 pregnene-3β-ol 20-one†	5	11 33	1 15	4 32	2 62	0 37	77 8
9	6 + 200 mg Δ^4 pregnene 17α,21 diol 3,20 dione†	5	19 48	1 95	8 48	3 15	0 21	70 2
10	6 + 200 mg Δ^4 pregnene 17α ol-3,20 dione†	6	15 99	2 67	6 54	2 80	0 13	76 3
11	No cortisone, only 3 gm MAG	3	16 14	2 35	5 22	7 98	0	94 2
12	250 mg compound F distributed over first 3 days	4	8 60	1 88	4 23	0 79	0	80 0
								Av 99 2%

* *Mono ammonium glycyrrhizinate*

† *Given I V on the 1st and 2nd day at level of 100 mg/day*

TABLE 3 *Formaldehydogenic substances (FS) in the urine of a normal middle aged male*

No Days	Total FS Mg 24 hrs	FS—Mg per 24 Hours			
		Most Polar Fraction A	More Polar Fraction B	Less Polar Fraction C	Least Polar Fraction D
7	6.71 ± 1.70	1.47	5.00	1.16	0.25
8	5.27 ± 0.60	0.99	4.40	1.[illegible]3	0.23
11	7.53 ± 1.08	0.77	3.90	1.40	0.61

polar (D) fractions from silica gel fractionation It can be seen that the sum of the FS values of the four fractions is between 70 and 132 per cent of the pre-chromatography FS value, with an average of 99.2 per cent This is in excellent agreement with the recoveries reported by Romanoff and others (D)

There is no correlation between the quantity of urinary formaldehydogenic substances and the daily dose of cortisone acetate in this case For example, in period 1 while receiving 25 mg of cortisone acetate plus 3 gm of MAG daily, and in period 5 while receiving 5 0 mg of cortisone acetate plus 3 gm of MAG daily the FS values were 15 62 and 16 92 mg 24 hrs respectively It is important to note that in the time comprising periods 6 and 11 inclusive (a total of 25 days) the patient was maintained on a daily dose of 2 5 mg of cortisone acetate plus 3 gm of MAG No correlation between the urinary FS values and the different steroids administered in each of the periods 7 to 12 can be found.

In table 3 are given the results of FS determinations on the urinary extracts of a normal middle aged man before and after the extracts were chromatographed on silica gel The FS excretion is fairly consistent in the three groups studied, comprising a 26-day period It can also be seen that most of the FS material is in the B or more polar fraction which contains steroids of the hydrocortisone type In each group the FS material is distributed in a definite pattern among the four fractions This is not true in the case of the adrenalectomized patient maintained on cortisone acetate plus MAG (see table 2 This discrepancy in the latter case may be due to a formaldehyde-producing substance in the urine possibly MAG

DISCUSSION

The level of 17-ketosteroids in the neutral fraction before and after adrenalectomy was approximately 2 to 3 times greater than that of the ketonic fraction obtained in the former on separation with Girard's reagent T In every analysis the neutral fraction produced an atypical orange [illegible] color which had a higher absorption at 420 than at 510 mμ The ketonic fraction on the other hand approached more closely the true Zimmermann color with higher absorption at 510 than at 420 mμ The Zimmermann reaction on the crude neutral fraction therefore does not give a true measure of the 17-ketosteroids in the urinary extracts The discrepancy in 17-ketosteroid [illegible] between the ketonic fraction and the crude neutral fraction especially in urinary extracts of patients with cancer of the prostate has been observed elsewhere [illegible]

It was also observed that no significant drop in 17-ketosteroid [illegible] in the urine of patient A after the first adrenal was removed The possibly may be explained by hyperplasia of the remaining adrenal with increased steroidal output After the second adrenal was removed, however, and the patient was maintained on cortisone acetate, there was a 30 to 50 per cent decrease in the 17-ketosteroid level of the ketonic fraction from the pre-adrenalectomy level The 17-ketosteroid data of the ketonic fraction of patient A also show that approximately 3 to 10 per cent of the administered cortisone acetate is excreted as 17-ketosteroids In patient B the data also show that mono-ammonium glycyrrhizinate does not contribute to the urinary 17-ketosteroid titre

In patient B no correlation could be made between the amount of cortisone acetate administered and the quantity of 17-ketosteroids excreted However, this finding may be explained in a number of ways This patient had one testis the 17-ketosteroid production from which may have varied enough from day to day to distort the correlation picture This is plausible since only 3 to 10 per cent of the cortisone acetate is excreted as 17-ketosteroids Since cortisone acetate was administered orally, the daily variation in absorption is another factor to consider Finally, the daily variation in utilization and in conversion of the administered cortisone acetate to other 17-ketosteroids cannot be overlooked For example, Hechter[6] has shown that the rat liver has a tremendous capacity for the conversion of corticosteroids He reports the formation of a number of products after perfusing desoxycorticosterone and cortisone through rat liver and places a conservative estimate at a minimum of twenty metabolic products

No correlation could be made between the urinary formaldehydogenic substances and the daily dose of cortisone acetate administered A possible explanation may be that he was receiving in addition 3 gm of mono-ammonium glycyrrhizinate daily This substance may very well be split into glycyrrhetinic acid and a uronic acid which in turn can give rise to formaldehyde with periodic acid oxidation

SUMMARY

The results of a study of the urinary steroid excretion of adrenalectomized subjects maintained on minimal doses of cortisone acetate together with mono-ammonium glycyrrhizinate are reported

The 17-ketosteroid titre of the neutral fraction before and after adrenalectomy was approximately two to three times greater than that of the ketonic fraction obtained from the former by separation with Girard's reagent T The neutral fraction always gave an atypical while the ketonic fraction gave a typical Zimmermann color reaction

Approximately 3 to 10 per cent of the administered cortisone acetate in adrenalectomized patients was excreted as 17-ketosteroids

The administration of ammonium glycyrrhizinate has no effect on the excretion of 17-ketosteroids in the adrenalectomized patient

No correlation could be made between the urinary formaldehydogenic substances and the daily dose of cortisone acetate administered to an adrenalectomized patient also receiving mono-ammonium glycyrrhizinate

The possible significance of these findings is discussed

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THE SIZE OF THE BLADDER ON INTRAVENOUS UROGRAPHY AND RETROGRADE CYSTOGRAPHY, A POTENTIAL SOURCE OF DIAGNOSTIC ERROR IN CHILDREN

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In the course of routine intravenous pyelography and retrograde cystography in the child, the bladder is frequently reported as dilated. Further complete investigation failed to reveal any basis for such a distended bladder. In an attempt to establish criteria for the normal or deviations of the normal bladder, a number of children were studied utilizing all the available techniques of urologic investigation.

METHOD

Clinical examination ruled out organic neurologic disease. Intravenous pyelograms, cystometry (using opaque dye for the fluid), cystogram and cystoscopy were carried out in the order mentioned. General anesthesia was utilized only for cystoscopy. Mild sedation was administered prior to the cystometric studies. Female patients were studied because of the relative ease in catheterization. At the moment that the patient expressed a desire to void, an x-ray was taken in order to correlate the appearance of the bladder with the particular reading of the cystometric curve.

CASE REPORTS

The following two cases are representative of those studied.

Case 1. A 10-year-old white girl was admitted to the hospital because of frequency of urination and persistent pyuria. Neurologic examination revealed no objective findings. Intravenous pyelography revealed normal upper collecting systems and what appeared to be a dilated bladder. Figure 1 shows the cystometric curve and initial desire to void at a pressure of 7 cm. H_2O with a volume of 200 cc fluid. Figure 2, *A* is the cystogram at this point. At a volume of 250 cc, the desire to void was severe, the intravesical pressure was 18 cm. H_2O. Figure 2, *B* demonstrates the size of the bladder at this reading. Cystoscopy revealed only a catarrhal urethritis, no evidence of bladder neck obstruction was seen.

Case 2. An 8-year-old white girl was admitted to the hospital with a diagnosis of pyelonephritis. In the course of a routine intravenous urogram (fig. 3, *A*) it was felt that the appearance of the bladder suggested some dilatation. Figure 4 is the cystometric curve. The first desire to void occurred at a volume of 200 cc with an intracystic pressure of 10 cm. of water. Figure 3, *B* demonstrates the bladder radiologically at this point. At 275 cc volume, the patient had an

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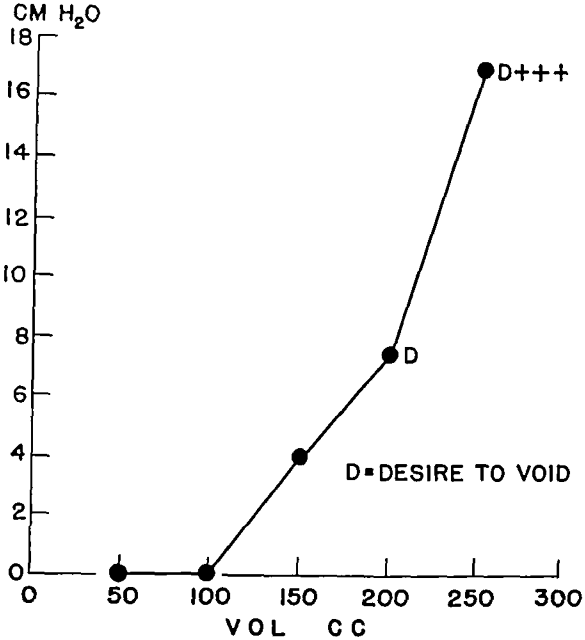

FIG 1 Case 1 Cystometrogram shows initial desire to void at pressure of 7 cm of water with volume of 200 cc fluid This is normal curve

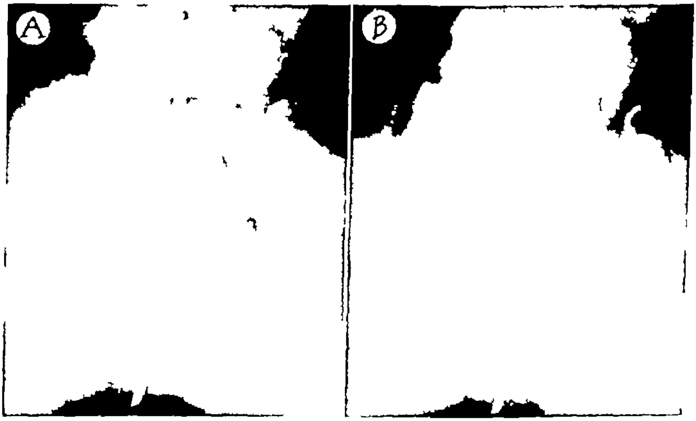

FIG 2 Case 1 *A*, cystogram taken at initial desire to void indicating seemingly distended bladder *B*, appearance of bladder on cystogram at pressure of 18 cm water and volume of 250 cc with marked desire to void This would appear to be a markedly distended bladder

increased desire to void and complained of minimal pain Cystoscopy and neurologic examination were completely negative

DISCUSSION

Radiographically, the bladders of the cases studied have the appearance of a distended or large bladder Critical analysis of the cystometric curves indicate that they are normal Campbell states that in children 8 to 10 years of age,

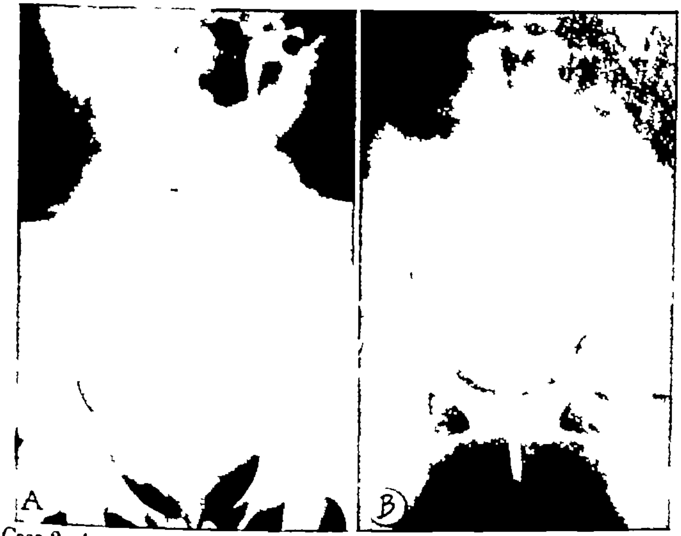

Fig 3 Case 2 *A* intravenous urogram suggests dilated bladder in 8 year-old girl *B* appearance of bladder on cystography at initial desire to void intracystic pressure being 10 cm. water at a volume of 200 cc

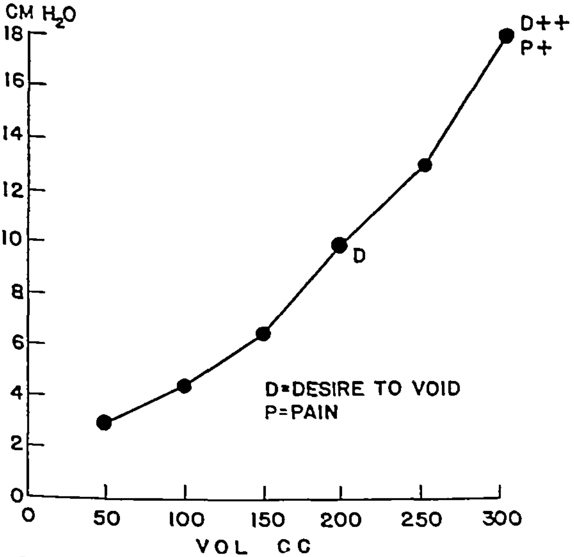

Fig 4 Case 2 Cystometrogram indicates first desire to void at 10 cm water pressure with bladder volume at 200 cc Normal curve

the initial desire to void occurs at a volume of 80 to 100 cc with an intravesical pressure of 9 to 11 cm H_2O ' The average physiologic capacity of the urinary bladder is about 100 per cent greater than the volume at which the first desire to void is felt and the anatomic capacity is usually more than twice this volume Our studies are in accord with this

In studying these cystograms, a smooth periphery is observed the longitudinal axis is greater than the transverse diameter The bladder outline is symmetrical Contrast this to the cystogram observed in the abnormal bladder whether it b so from myogenic or neurogenic causes Here, there is irregularity of the periphery, evidence of trabeculations, there may be asymmetric outline and there ma also be a globular outline seen so frequently in the markedly hypotonic or i the atonic bladder

The appearance of the normal bladder in the child, radiographically, ca best be explained by correlation with its embryologic development In the sixth week of fetal life, the urorectal septum has divided the cloaca into an anterio vesicourethral segment and posterior rectal portion The ureteral stalks and wolffian ducts lead from the vesicourethral division, the upper portion of which becomes the urinary bladder while the lower or inferior portion becomes the posterior urethra in the male, and the urethra in the female The bladder is a hind gut structure of entodermal origin while the trigone is of mesodermal origin In the infant, the bladder is an abdominal organ partly because of its tubular urachal derivation and partly because the distended viscus is too long for the comparatively small pelvis As the child grows, the bladder will gradually settle into the pelvis This process of "dropping" into the pelvis is not yet complete in the 10-year-old child This results in the relative disproportion between the bony pelvis and the bladder which appears as if distended This explains also the greater vertical diameter as compared to the transverse plane

In conclusion this report indicates that

The so-called distended bladder in the child is not of pathologic significance unless the criteria described above are associated with the distension

The normal capacity of the urinary bladder is from 100 to 200 cc in this age group

The appearance of the normal bladder differs from the abnormal in 1) the greater longitudinal axis, 2) symmetrical enlargement, 3) the lack of the usual objective findings seen in those x-rays where neurogenic or myogenic disease may exist

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STERILE FLUOROSCOPY PRELIMINARY REPORT OF A NEW TECHNIQUE FOR LOCALIZATION OF RENAL CALCULI

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Since the first nephrolithotomy, the elusive renal calculus has given generations of urologists hours of anguish, and has left a trail of discontented surgeons with memories of unintended nephrectomies, traumatized kidneys, and indeed, unfound stones

Many methods have been advocated and devised to localize and extract renal calculi Several are of great benefit, but many leave much to be desired

Roentgenograms taken preoperatively and at the operating table are of great benefit However, a surgeon needs only one experience in attempting to transpose the location of a stone in a roentgenogram to the kidney on the operating table, before he realizes how difficult this may be

Other methods include mechanical stone finders which are costly and do not seem to obtain the results desired by all Needling is an old and very often fruitful maneuver, but not without renal damage in proportion to the times used Even with needles in place a roentgenogram only too often fails in localizing a calculus Other well used methods include rigorous irrigation, fibrinogen netting, sounding, palpation, and, of course, nephrotomy Several of these maneuvers are useful and frequently successful All of these procedures, however, were devised to overcome the deficiency of direct visualization of the stone

In the past fluoroscopy has been used in an attempt at direct visualization of renal calculi[1-3] Braasch and Carman,[4] realizing the inadequacies of roentgenograms and other methods to visualize stones, and stressing the importance of preservation of renal tissue, have reported the use of fluoroscopy at surgery They used a portable machine, and an unsterile fluoroscopic screen at the side of the operating table During the examination a sterile rod was used to point to the stone This technique is unsatisfactory to most urologists for several reasons The size of the machine and screen is cumbersome and is unable to be placed in the sterile field The image produced is distorted and not clear due to the long object to screen distance Higher power is needed to penetrate the tissues increasing the radiation hazard Further, the operation could not continue simultaneously with the fluoroscopy In spite of these disadvantages, the introduction of fluoroscopy to surgery was considered a great step forward

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Read at annual meeting, American Urological Association, Pittsburgh, Pa , May 6–9, 1957

Note by Editor Doctors Baskin, Harvard and Janzen's exhibit on sterile fluoroscopy at the 1957 meeting of the American Urological Association was awarded first prize by the Committee to Judge Scientific Exhibits, Dr John A Benjamin chairman

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With these factors in mind, and the goal of direct visualization of the calculus during surgery, we have devised an instrument and technique of sterile fluoroscopy which we believe helps to overcome these problems

NEW TECHNIQUE

A small sterilizable unit consisting of a fluoroscopic screen and protective lead glass which is entirely enclosed in transparent plastic has been constructed It may be placed in the wound immediately adjacent to the kidney A sterile steel radiographic cone is adapted to a portable x-ray machine and brought to the opposite side of the kidney When the room is darkened and the x-ray tube is energized, the surgeon may localize the calculus under direct fluoroscopic vision (fig 1)

Screen A high contrast and high definition fluoroscopic screen is mounted on a piece of lead glass, both of which are permanently sealed in a durable, transparent plastic container The unit is rectangular and measures 10 by 7 5 by 1 5 cm Its edges are rounded and smooth to protect tissue from trauma Although we have elected this size from our experiences, other sizes and shapes may be desirable See figure 2

Sterilization is accomplished by immersion in aqueous zephiran for 20 minutes, which is harmless to the unit Investigation is currently under way to develop a unit which may be sterilized by autoclaving

X-ray cone A steel cone was devised to fit the head of our portable x-ray unit It is telescopic, extending from 19 to 35 inches (48–89 cm) and has a 2½ inch (6 5 cm) diameter A lead diaphragm with a 1 cm diameter aperture is located in the proximal end Adaptable lead diaphragms may be capped on to the distal

FIG 1 Showing surgeon localizing calculus Fluoroscopic screen is in wound Radiologic covered with sterile cloth, is on opposite side of kidney

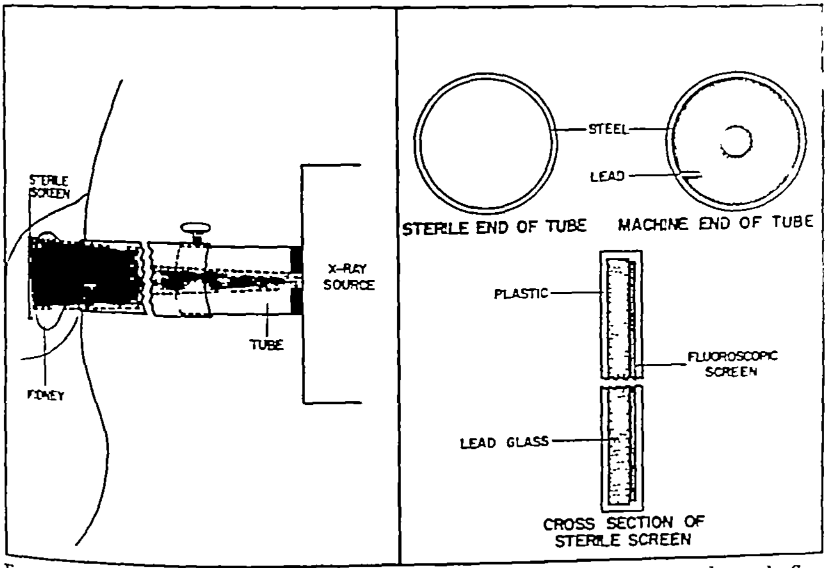

Fig 2. A, diagram of technique B, sketch of radiographic cone (tube) and sterile fluoroscopic screen

end to vary the size of the energizing beam This tube may be made sterile by autoclaving or by covering it with a sterile cloth

The length and construction of the cone confine the x-ray beam and minimize radiation hazard Since it is sterile, it may be placed immediately in contact with the kidney

X ray equipment We have used a standard portable Picker machine which has a timer allowing a maximum of 14 seconds per exposure

Power 80–60 K V P and 1–2 M.A have been used, with excellent results We have found that this can usually be reduced if the kidney is delivered well and the x-ray beam need not penetrate any tissue except the kidney

Distance A focal spot to target distance of 30 inches (76 cm) has been used This may be varied with the telescopic cone

Object size We have visualized calculi as small as 0 25 cm It would be difficult to estimate the smallest stone that could be seen due to variability in composition Surgical needles are sharply seen

Kidney clamp A wire clamp with long handle has been used to manipulate the kidney This, however, is not essential Immobilization of the kidney by means of supporting sponges has proved most satisfactory

RADIATION HAZARD

The radiation hazard to personnel using fluoroscopy is well documented so that manufacturers of x-ray equipment provide the means for safe and proper use of the x-ray beam during fluoroscopy Since these mechanical features require a rigidity of discipline not feasible in the operating room, we explored the radiation dosimetry of the present equipment under actual operating room conditions

The effectiveness of the beam limiting extension cone was first determined Without the cone, readings in the operative field and over six inches off the beam center were above 200 milliroentgens per minute (mr/min) Obviously a proper extension tube had to be used to reduce this to a safe limit

Next the effectiveness of the lead glass was determined When the screen and glass were in position to intercept the entire x-ray beam the readings were zero (unreadable) mr/min directly behind the glass

Scattered radiation was then measured when 1) only the kidney lay between

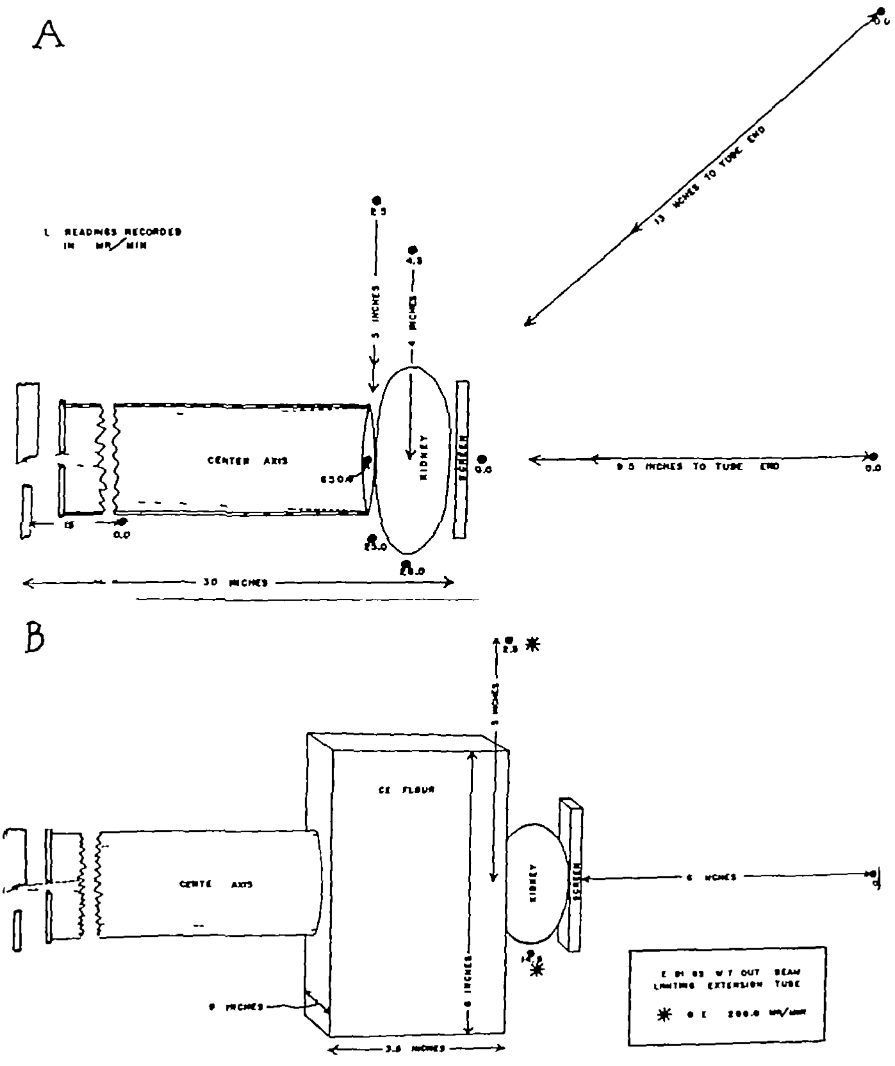

FIG 3 *A*, measured radiation scatter in milliroentgen units per minute when only kidney lay between viewing screen and cone *B*, showing radiation scatter in milliroentgen units per minute at varying distances when x ray beam passes through skin, muscle, fascia and kidney

[illegible] and the viewing screen [illegible] A [illegible] and its [illegible] B). Figure 3 A and B show the [illegible] the hands and the readings [illegible] from the kidney. The [illegible] distance [illegible] to personnel. However, since the [illegible] measured, we can note only that [illegible] the currently accepted tolerance limits.

The principal danger probably lies in having the lead glass [illegible] intercept the entire x-ray beam. The dose rate then [illegible] since the observer's eye is likely to be close to the [illegible] is much more susceptible to damage and cataract formation. [illegible] of the extension tube should be limited so that the diameter of the [illegible] beam will not exceed the smallest diameter of the lead glass. Under [illegible] conditions small diameter tubes should be used.

In brief, the radiation hazard appears to be well within tolerable limits when 1) an appropriate beam limiting cone is used, 2) an adequate lead glass screen is used, 3) rigidity of cone and screen alignment is provided, and 4) economical time and kilovoltage-milliampere factors are used. If these conditions cannot be met it would be unwise to undertake this procedure. There is no excuse for inviting damage to the hands, eyes, and health of personnel by not abiding by the above conditions.

DISCUSSION

It is believed that this new technique offers the following advantages:

The screen can be sterilized and is small enough to place in the wound.

Because of the proximity of the screen to the kidney, there is minimal distortion of the image.

The total field is 2½ inches (6.5 cm.) or less in diameter, allowing good visibility.

The tube can be made sterile and placed in the operative field.

Scatter is reduced to a minimum. Low radiation levels can be used when only the kidney is penetrated. When the kidney cannot be readily mobilized and x-rays may have to penetrate part of the abdominal wall, slightly higher voltages are needed.

The apparatus is simple and requires only three essential parts: the sterile screen, the cone, and a portable x-ray machine.

It is inexpensive. Only the cone and screen must be obtained, as most hospitals own portable x-ray machines.

The same x-ray machine used for fluoroscopy can be used for routine roentgenograms at surgery.

The use of the technique may shorten the operative time. This may be of the utmost importance in poor anesthetic risks.

Its disadvantages brought out at clinical trials are:

The lights must be turned off for maximum contrast and brightness. To avoid too much darkness a red light may be used in the room and the entire procedure should require only a few minutes to identify the stone

Dark adaptation and accommodation should be used Although the recommended time for this is 20 minutes, in actual clinical trials calcific stones were visible without any adaptation However, for maximum efficiency and a minimum of radiation, one person of the surgical team should drop out and adapt for this time No time need be lost if the remaining members of the team continue the operation Even if the whole operating team were to adapt for 20 minutes, it would be a short period compared to the time spent in searching which might ensue without fluoroscopic aid

There are a few prerequisites to obtain the best results The incision must be adequate The kidney should be dissected as free as possible allowing maximum delivery The kidney may then be raised by placing sponges below it or it can be manipulated with a specially designed wire support The cone may then be placed directly on the organ

The anesthetist should be consulted concerning the use of electricity in the room

Clinically, we have found sterile fluoroscopy very promising It has been used to locate a calyceal diverticulum as well as renal stones In the former instance the pelvis was injected with sterile radiopaque solution to visualize the diverticulum A calyceal diverticulectomy was then done with minimal renal tissue sacrifice Once visualized, the position of a stone has been kept identified by placing a needle down to it under direct fluoroscopic vision Appropriate surgical steps were then taken

We are hopeful that this technique of fluoroscopy can be adapted to other fields such as orthopedics, foreign body removal, and visualization of other tubular structures This technique may be of great value for the military in removing shell fragments

We feel that in our brief experience with this new technique a valuable adjunct to localization of renal calculi at the operating table has been added

SUMMARY

A new sterilizable fluoroscopic screen and the technique for adapting it to use in a sterile surgical field are described with particular reference to its use in localization of renal calculi Radiation hazards are discussed Its advantages and disadvantages as demonstrated in clinical application are presented

We wish to express our appreciation to Mr Paul Rosenbaum for his original survey of dose rates, and to Dr Richard Barach for his complete survey of these

We also wish to express our appreciation to Mr Laurence E Cowles, R T A S X T and Mr Louis Divilio, R T A S X T, chief x-ray technicians of the New Haven Unit and Memorial Unit Radiology Departments, respectively, of the Grace-New Haven Community Hospital for their co-operation and technical assistance

The co-operation and efforts of the Radelin Division of the United States Radium Corporation of Morristown, New Jersey, in manufacturing this instrument are sincerely recognized

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A SELF-RETAINING RETRACTOR FOR USE IN SURGERY OF THE RETROPERITONEUM

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In surgery the exposure of deep-seated organs such as kidneys or adrenals is difficult in obese patients. Two methods of retraction have been used as aids: 1) manual retraction by an assistant using large abdominal retractors, and 2) insertion into the wound of self-retaining Finochietto retractors. Both of these methods have limitations. At times a second assistant may not be available, and even if one is present, he must hold the instrument against an unyielding rib cage. This trying position cannot be maintained for too long an interval and as a consequence, frequent annoying shifting of the appliance results. The other aid, the Finochietto retractor, is useful when it stays in place, but it frequently falls out of the wound, as in the type of wound prepared to expose a kidney or adrenal, the lower edge is soft tissue and the retractor cannot be anchored properly. Also, especially in obese patients, the relatively short arms of the Finochietto retractor do not permit adequate visualization in the depths of the wound, the areas where the adrenal gland and the renal pedicle are situated.

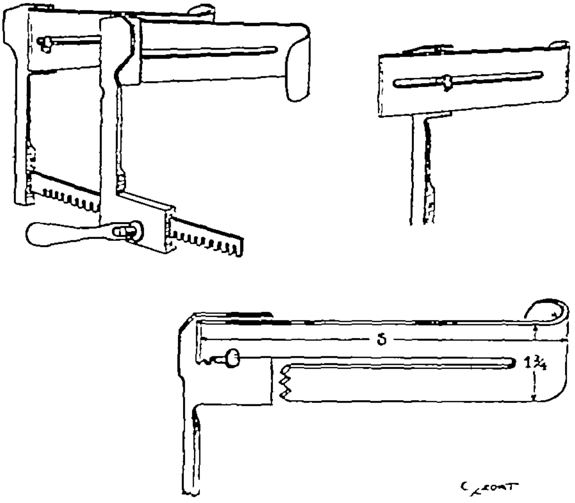

FIG. 1

To overcome these shortcomings a modification of the Finochietto retractor was designed.* Movable side arms with curved edges were placed into each wing of the Finochietto retractor. These are lowered a specific distance, variable in

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* Manufactured by Codman and Shurtleff, 105 Brookline Ave., Boston 15, Mass.

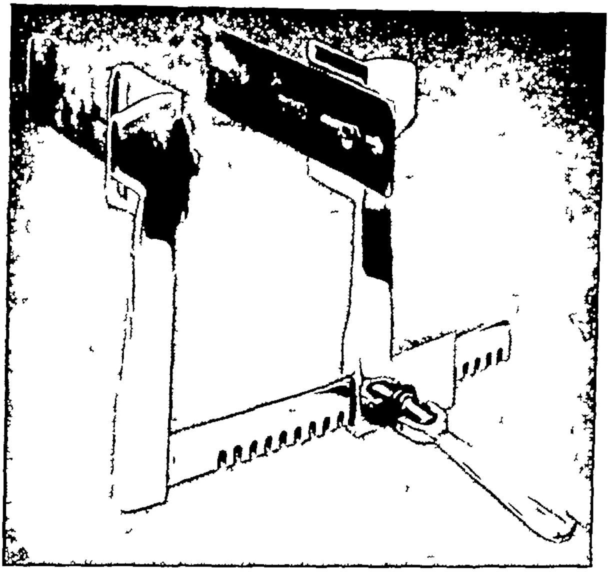

FIG 2

each patient, in order for the arms to reach the depths of the wound (figs 1 and 2) The side arms are then locked in place by a set screw

The retractor has been used in the following manner After the wound is prepared (frequently after rib resection) the side arms are lowered and secured, and then the Finochietto rachet is used to enlarge the wound The deep arms stabilize the instrument and prevent its falling out of place In our experience, however, *the retractor has not been useful in shallow wounds or in thin patients* Here the depth is not sufficient to allow proper stabilization But the retractor was not designed for this work Nevertheless, if a second assistant is not available, the tool will provide a better exposure than can be obtained in many instances with only one assistant, even in thin patients

The wound necessary for exposure of the adrenal provides a space deep enough to stabilize the retractor in all patients During the operation of simultaneous bilateral adrenalectomy by two surgical teams the appliance is especially useful as it permits surgery to proceed without the presence of second assistants, allowing for less crowding at the operating table

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